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ORIGINAL ARTICLES

CLINICAL OBSERVATIONS ON NINETY CASES OF ACUTE
EPIDEMIC POLIOMYELITIS

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OF NEW YORK.

(From the Hospital of the Rockefeller Institute for Medical Research, New York.)

IN June, 1912, Peabody, Draper, and Dochez¹ published a report on 71 cases of acute epidemic poliomyelitis admitted to the Hospital of the Rockefeller Institute for Medical Research during the summer of 1911. During the summer and autumn months of 1912 and 1913, 90 cases were admitted to the Hospital, 57 in 1912, and 33 in 1913. The present paper reports the clinical observations made on the 90 cases admitted in 1912 and 1913, that seem to have importance from the fact that attention has not been drawn to them in earlier clinical accounts.

Cases were admitted during the acute stages only, and, after having remained in the hospital for from a few days to three months, they have reported at intervals since for observation and advice as to treatment. A far larger number were seen in the dispensary and were not admitted, as the acute stages were passed. In addition to the 90 cases admitted during 1912 and 1913, 7 cases were admitted on the possibility of their condition being due to acute poliomyelitis. The steady decrease in the number of admissions was due to a decrease in the number of cases of the disease in New York, and in addition to the decrease in numbers, a decrease in severity was observed, for in the 71 cases admitted

¹ A Clinical Study of Acute Poliomyelitis. Monograph No. 4, June, 1912. The Rockefeller Institute for Medical Research.

during 1911, Peabody, Draper, and Dochez reported a mortality of 14 per cent., while among the 57 cases admitted during 1912, the mortality was 16 per cent., and among the 33 admitted during 1913 it was 9 per cent. Furthermore, the 3 fatal cases of 1913 died of secondary inflammatory conditions of the lungs, and not directly from the disease. The resulting paralyses, however, were as widespread and complete in 1913 as in the previous years.

ETIOLOGY. The ages of the patients varied from nine months to fourteen years. In three instances two members of a family were admitted, and in a fourth instance two cousins living in the same house. It was further observed that although only in a very few instances could a direct or indirect contact with a patient suffering from the disease be recorded, at any one time the majority of patients came from the same general locality in New York. Inquiries were made as to the prevalence of flies and other insects in the house, and subsequent to the communication of Rosenau² on the conveyance of infection by the stable fly (*Stomoxys calcitrans*), the proximity of the home to stables was in all cases inquired into. Neither the prevalence of insects nor the neighborhood of stables was found to be a usual occurrence. In many cases the parents suggested some slight accident or some dietary indiscretion as the cause of the condition, but in no case could a predisposing cause be ascertained.

In view of the possible importance of the nose and throat as the point of entrance of the infection, the tonsils were in all cases inspected.³ Simple inspection is unsatisfactory in estimating the size or condition of tonsils, but in 37 cases they were noted as somewhat enlarged and congested, in 18 cases as enlarged, and in 4 as slightly congested. In the remaining 31 they were noted as normal or were not examined, as occurred in two rapidly fatal cases. In the case of 8 children whose tonsils were noted as enlarged and congested, 21 other children in their families were examined, and of these in 16 the tonsils were noted as showing no enlargement or congestion. In 15 cases the tonsils were enucleated, and on removal usually proved to be larger than inspection had led one to expect.

SYMPTOMATOLOGY. 1. *Preparalytic and General.* While no cases were admitted in the preparalytic stages, 5 abortive cases were admitted, and in 22 cases the paralysis increased after admission to the hospital. The preparalytic and general symptoms were in all cases inquired into, and are important in view of early diagnosis. These symptoms were observed by the parents or attendants for from a few hours to nine days before the onset of paralysis, but all of them were further observed in the cases after

² International Congress of Hygiene and Demography, Washington, 1912.

³ Leiner and Weisner, *Wien. klin. Woch.*, 1910, xxiii, p. 323; Flexner, S., *The Contribution of Experimental to Human Poliomyelitis*, Jour. Amer. Med. Assoc., 1910, lv, pp. 1105-1113.

admission to the hospital and might continue until the acute general symptoms passed off. The most common symptom was *feverishness*, and this was reported to be present in 79 of the cases. It was not constant, but might appear for a day or two and then disappear before the onset of paralysis, or it might appear only after the onset of paralysis. In the records of the temperature (rectal) after admission a high temperature was exceptional, and while one case was admitted with a temperature of 104.8° , and in the fatal cases temperatures of 104° to 105° were observed before death, a temperature that varied from 101° to 103° and gradually settled in the course of a few days was seen in the majority of cases. The temperature may be settling some days before the cessation or spread of paralysis, but it was usually still slightly elevated for some days after further spread of the paralysis was observed. A child, aged three years, was readmitted for observation four months after the onset, and at that time an afternoon temperature of 100° or over was of daily occurrence, although there was no evidence of a recurrence or of any other cause of an elevation of temperature. The pulse rate did not, as a rule, settle until some days after the temperature was normal, and in a few cases showed the irregularities of sinus arrhythmia. The pulse rate was commonly between 120 and 140 on the day of admission. *Drowsiness or heaviness* was noted in 47 cases, and this was very variable in degree, for sometimes an apparently comatose condition was present, from which, however, the child could be readily aroused. Accompanying this heaviness there was a condition of *irritability or restlessness*, best seen when the child was aroused, and frequently connected in the older children with fear of pain consequent on handling. The restlessness was also observable during sleep, the child tossing about and rolling the head from side to side. In spite of the drowsiness the children seldom slept well, being wakeful and querulous, and this was in marked contrast to the sound, uninterrupted sleep seen in early convalescence. During sleep, definite involuntary *twitchings or jerking*s were seen in 20 of the patients. These jerking were seen as short, sudden movements either of flexion or extension of a limb, and frequently in a limb that subsequently became paralyzed. The movement might involve upper and lower limbs on one side of the body, both lower or both upper limbs, or all four limbs, or head and neck, or the whole body at once. A totally paralyzed part never showed such movement, but it was most frequent in a limb that showed a slight weakness. It was not observed after the acute general symptoms passed off. A fine tremor was seen in a few of the patients similar to that described by Netter and others.⁴ A lateral nystagmus was seen in one patient, and though not

⁴ Paralyse infantile choreique, Arch. de Méd des Enfants, December, 1913.

constant, it was present without any voluntary movement of the eyeballs. A history of a localized, profuse *sweating* was occasionally obtained, involving the part that subsequently became paralyzed, but more common was profuse general perspiration in the very severe cases. This general perspiration occurred both when the child was awake and when it was asleep, but was usually more profuse during sleep. It did not cease with the other acute symptoms or with the fall of temperature, and in one case was still well marked, though diminished, at the end of six months.

Gastro-intestinal symptoms were rarely absent, and vomiting was reported in 41 cases and loss of appetite in 22 others. Diarrhea,⁵ which has been reported as common in some epidemics, was rarely given as a symptom, and was noted in only 7 cases, while constipation was a marked feature in 38 of the patients. After admission the patients in the acute stages were very thirsty, but had no appetite for solid food. When the acute symptoms disappeared, the appetite returned at once and was usually vigorous. Convulsions occurred only once, and rigors were never noted.

A symptom of considerable importance, in that it is observed early and that it is not present in gastro-intestinal disturbances, nor, as a rule, in the common infectious diseases, is the *stiffness of neck and back*, resistance to anterior flexion of the neck and back, or pain on attempting such flexion. This was present in 72 of the cases, and persisted for from one day after admission to three or more weeks. Of the 18 children who did not show this resistance, in 7 the posterior muscles of the neck and back were paralyzed, and the others were mild cases or were seen for the first time late in the disease. In three instances there was definite head retraction, with arching of the back, and in several more the patient was restless unless placed in a position that would allow of slight arching or retraction. This symptom was present to a marked extent in cases with only slight paralysis, and was the most marked feature in two cases classed as abortive. On the other hand, cases with extensive or severe paralysis showed slight stiffness and resistance to anterior flexion, and there was no relation between the degree of abnormality of the spinal fluid and the degree of resistance.

Pain and tenderness are important symptoms of the acute stage, and are sometimes observed before any paralysis is noted. Tenderness on handling was noted in 61 of the cases, and many more showed signs of pain when neck and back were flexed. In many cases the tenderness on handling was due to flexion of the neck and back, but in others it had no connection with such movement. It might be generalized and cause the child to dread the approach of anyone likely to handle him. In other cases it was localized

⁵ Krause, P., *Deut. med. Woch.*, 1909, xxxv, 182.

to a limb or limbs, usually the parts paralyzed. This tenderness during the acute stages seemed to be of three types or degrees. In a few cases a hyperesthetic condition of the skin was suspected, but in dealing with patients of the age and condition under observation, accurate determination of such a point is difficult. In a few others, mild pressure on the muscle masses caused pain, not specially localized over the nerve trunks. In many more, passive movements that would stretch tendons or capsular structures caused the child to cry out with pain. This tenderness was seen frequently in limbs, that at no time showed paralysis, but the deep reflexes were usually absent. On the other hand, it could be elicited in limbs that were totally paralyzed. It frequently caused a child to keep a limb that was not paralyzed at rest and simulate paralysis, the true condition of the limb being ascertained only by handling. This tenderness, as a rule, passed off in a day or two, but might persist for three or four weeks. It constantly persisted after further spread of paralysis was noted, and passive movements increased rather than decreased its severity. After the acute stage was passed a different type of pain on passive movement was observed. If a limb were allowed to remain at rest after the acute stage, the capsular structures, tendons, and muscles appeared to stiffen, and in these cases the tenderness decreased with treatment by passive movements. This tenderness was usually localized more to the region of joints, and occurred in joints the muscles controlling which were completely flaccid as well as at joints where the muscles were only partially affected, and simulated the joint pain of an arthritis, but without local points of tenderness on pressure. Yet another type of tenderness must be noted. Some weeks after the onset a limb that has hitherto shown no sign of paralysis becomes painful on movement, the child does not use it freely, and the part appears to be paralyzed. This was well seen in a child whose left upper limb alone was paralyzed. Three weeks later, when the child was allowed to run about, she complained of pain in the knees and seemed unable to walk. On admission it was found that the muscles of both lower limbs were spastic and that the tendon reflexes were all exaggerated. The pain was situated in the flexor tendons at the back of the knees. Massage and movements relieved the stiffness, and the pain disappeared. It is possible that in such cases irritation to the pyramidal tracts results during the healing process of the lesion in the upper part of the cord.

Spontaneous pain is difficult to ascertain in patients of the age usually affected, and frequently what appeared at first to be spontaneous pain would disappear on adjusting the position of the patient to avoid tension on muscles or ligaments. In one case the pain could not be relieved by adjustment of position and seemed to be independent of such adjustments. This pain disappeared

with the other acute symptoms. In this case, a girl, aged four years, there was present for two days after admission an apparent absence of sensibility to painful stimuli, as pricking with a pin caused no response, but the child was in a comatose condition at the time, and the sensibility returned as the coma passed off and the spontaneous pain manifested itself.

2. *Paralysis.* Wickman⁶ has differentiated eight types of the disease, based on the fully developed symptomatology. The distinction between these types depends on the localization of the lesions in the central nervous system. Any part of the brain and cord may be affected, and in any one case the lesions may be widespread, or lesions may be present giving at one time a paralysis of the muscles of the face and of a lower limb. The different types cannot then be rigidly differentiated, and the distinction between the meningeal and the abortive types is often extremely difficult. Müller⁷ classifies all cases that do not show definite paralysis as abortive, and it is simpler to adopt his classification in this respect. Of the paralyzed cases, the differentiation of bulbospinal and cerebral types has been suggested, and though rarely cases of definite spastic paralysis are found, it is more common to find spastic and flaccid conditions coexisting.

Involvement of the *respiratory* musculature is of importance in its prognostic significance; 11 of the 12 fatal cases may be included in this group. In 7 of them death was due directly to the respiratory embarrassment, and in the remaining four it was due to secondary inflammatory conditions in the lungs. In 1 other fatal case death was due to an inflammatory condition of the lungs secondary to a paralysis of the muscles of the palate and pharynx. Of the 31 cases showing involvement of the muscles of respiration, there was paralysis or weakness of both diaphragm and intercostals in 9, and of these, 6 ended fatally while in the hospital. In 3 cases the diaphragm alone was involved without complete paralysis, and in each instance there has been complete recovery in the action of the diaphragm; 19 cases showed paralysis, complete or partial, of the intercostal muscles, and of these, 3 ended fatally and 7 recovered entirely. In no instance was the respiratory paralysis the only paretic symptom. The prognosis as to life is always grave when the respiratory musculature is weakened, and though severe paralysis of the kind is readily observed, a weakness of either diaphragm or intercostals is easily overlooked and may be the commencement of a spread that will terminate fatally. Rapidity of respiration is not necessarily present with slight weakness or limited paralysis, as either the diaphragm alone or the intercostals alone are able to carry on efficiently the movements of respiration, and even when

⁶ Beiträge zur Kenntniss der Heine-Medinschen Krankheit, Berlin, 1907.

⁷ Die Spinale Kinderlähmung, Berlin, 1910.

present, the rapid, shallow respirations may be erroneously considered part of the general acute condition. If the chest is prevented from expanding by pressure on the thoracic wall, a weakened or asymmetrical action of the diaphragm can be estimated by observing or palpating its movements in descending and ascending in the abdomen, while pressure on the abdomen to limit or prevent the descent of the diaphragm will demonstrate the power of the intercostals to carry on respiration by expanding the thorax. As with any part of the body musculature, weakness of the diaphragm and intercostals may appear and disappear again in the course of a few hours.

The large number of cases showing involvement of *facial* muscles was striking. Of the 90 cases, 31 showed weakness of the muscles of the face, and in many more a slight involvement was suspected. In 5 cases this was the only paretic symptom, while in the remaining 26 other parts of the body were involved. In 1 case, which showed many unusual factors and which will be discussed more fully later, the weakness of the facial muscles was bilateral. In 7 cases the whole of the muscles of one side of the face were paralyzed. The others, while showing a definite asymmetry, showed a weakness of the whole of one side or a paralysis or weakness of the upper or lower parts of the facial musculature only. Of the 5 uncomplicated cases, 3 showed a definite exaggeration of the tendon jerks in the upper and lower limbs, in a fourth the tendon reflexes seemed normal, and in the fifth the tendon reflexes of the upper limbs were diminished, while those of the lower limbs seemed normal. Among the cases complicated by paralysis of other parts of the body, spasticity and exaggerated reflexes were occasionally met with, but not to a greater extent than among cases showing no involvement of cranial nuclei. In the case of a girl, aged three years, admitted on the fourth day after the onset of symptoms and the third day after the appearance of paralysis, and showing involvement of the left side of the face, of the laryngeal and pharyngeal muscles, and to a slight extent of the respiratory musculature, all the tendon reflexes were exaggerated on admission. Without any paralysis of the extremities developing, the tendon reflexes gradually diminished and were lost in the course of the next two days until the only one obtainable was the right Achilles reflex, and it was but a feeble response. In 3 cases the facial weakness cleared up in the course of a few weeks, and in 5 of them no sign of facial involvement was apparent after an interval of from three to six months. At the end of that time 3 had shown no improvement, while 16 showed distinct improvement, and the remaining 4 died during the acute stage of respiratory involvement. One case deserves special notice in that an almost complete ptosis of the right upper eyelid was the only paretic symptom on admission, though when seen again six months later, slight weakness of the

lower part of the face on the right side and of the right external rectus could be demonstrated, while the ptosis had almost entirely disappeared.

Difficulty with *micturition* is fairly common, and is probably due to a local rather than to a general weakness, for it occurs in cases that show slight paralysis of the limbs as well as in severely paralyzed cases and in cases that show few general symptoms. The difficulty of *defecation* is usually associated with the paralyzed or weakened muscles of the abdominal wall, but in one case the anal sphincter was observed in a patulous condition for a few days.

3. *Abortive Cases.* Five of the cases were considered to be examples of the abortive type. In 3 no history of direct or indirect contact was obtainable, and the illness commenced with fever, vomiting, or loss of appetite and constipation, with in 2 cases general weakness and twitchings of the limbs and pains in the knees. On admission all three showed marked stiffness of the neck and back, and their spinal fluids contained 101, 34, and 9 cells respectively per cubic millimeter. The fluid with 9 cells per cubic millimeter contained a marked excess of globulin, and in all the mononuclear cells predominated. No paralyzes were discoverable, though some of the tendon reflexes were exaggerated and others diminished, and nothing suggestive of any of the common acute infections in children was found. Two of them recovered entirely in the course of a few days, while the other was somewhat stiff and ataxic for four weeks. The fourth case was that of a boy, who lived in the same house with his cousin, admitted at the same time with paralysis. He was feverish and irritable at the commencement, and on admission, four days later, showed marked head retraction, but no characteristic changes in the spinal fluid. No paralyzes were observed, and he had completely recovered three weeks later. The fifth case was the brother of a child admitted two days previously with paralysis, and he was admitted after a typical history of onset, with a temperature of 103.4°, no stiffness of the neck, but with 89 cells per cubic millimeter in his spinal fluid. In the course of two weeks his spinal fluid became normal, but he remained heavy and did not recover his appetite or his spirits. No tubercle bacilli were found in his spinal fluid, but he died three months later with a rapidly terminating tuberculous meningitis. It is possible that the original diagnosis of acute poliomyelitis was incorrect in this case.

Diagnosis. In the preparalytic stages and in abortive cases the diagnosis of acute poliomyelitis is always a matter of difficulty, and until some specific bacteriological or immunological test is devised, reliance must be placed on the general symptoms and on the character of the spinal fluid.⁸ The occurrence at the time of an

⁸ Peabody and Draper, A Study of Cerebrospinal Fluid and Blood in Acute Poliomyelitis, Amer. Jour. Dis. of Children, 1912, iii, p. 153. Fraser, F. R., A Study of the Cerebrospinal Fluid in Acute Poliomyelitis, Jour. Exper. Med., 1913, xviii, p. 242.

epidemic is strong evidence in a case where the diagnosis would otherwise be doubtful. The character of the spinal fluid in other acute infections is not at present sufficiently established for much reliance to be placed on the results of lumbar puncture in ruling out such infections. In its gross characters, in the cytology and in globulin content, the spinal fluid in tuberculous meningitis and in syphilitic myelitis closely resembles that seen in acute poliomyelitis, while the clinical features of these two diseases are often indistinguishable. This is well illustrated by two cases that follow:

CASE I.—L. B., a boy, aged two years and three months, had been a full-time child, difficult to bring up, but without any previous history of congenital syphilis. He was admitted with weakness of the right side of the face, right arm, and right leg, setting in after four days of drowsiness, fever, and gastro-intestinal disturbance. The paralysis was flaccid, there was no impairment of sensory functions, and there was definite stiffness of the neck. The child gave evidence of congenital syphilis in the bones of the skull, thorax, and limbs. The spinal fluid on admission contained 560 cells per cubic millimeter, mostly lymphocytes, and gave a heavy flocculent precipitate with the Noguchi test. The fever disappeared in a day or two, but the cells in the spinal fluid increased until a week after admission, when 1600 per cubic millimeter were present. The Wassermann reaction in the spinal fluid was positive, which is not found to be the case in acute poliomyelitis, and it was strongly positive in the serum also. He was transferred to the Babies' Hospital, and there the paralysis cleared up to a large extent after the intravenous administration of salvarsan.

CASE II.—W. L., a boy, aged twenty-two months, was reported to have been perfectly well until four days before admission, when he became feverish, vomited, was constipated, and his legs were paralyzed. On admission there was a flaccid paralysis of most of the muscles of the left leg. In the course of the next few days the paralysis spread to the right leg, to the face, to the external rectus of the right eye, and, to a slight extent, to both arms. On admission the spinal fluid contained 93 cells per cubic millimeter, and on the day of death, which occurred three weeks after the onset, it contained 451 per cubic millimeter, and tubercle bacilli were found in considerable numbers. No autopsy was obtainable, but before death the clinical picture was strongly suggestive of tuberculous meningitis. The cells were mostly lymphocytes, and the globulin reaction gave a definite precipitate, and, as in the previous case on admission, the clinical aspect and the findings in the spinal fluid were very similar to those seen in acute poliomyelitis.

From the pathology of the disease it is possible that a lesion causing recognizable clinical signs may occur in any part of the brain and spinal cord. In 3 cases where unusual clinical signs

were present, a diagnosis of acute poliomyelitis was made. The cases occurred during an epidemic, and no other satisfactory diagnosis was supported.

CASE III.—A girl, aged nine years, was admitted after three days of slight feverishness, vomiting, and headache, with paralysis of the left side of the soft palate. The spinal fluid was normal, the child seemed quite well, and nothing else was discovered on physical examination. No diphtheria bacilli were found in the throat, and the condition of the palate cleared up in the course of two or three weeks. Serum from this patient protected a monkey from an intracerebral injection of poliomyelitis virus.

CASE IV.—The case of C. W. was diagnosed as polioencephalitis. The child was a boy, twenty-one months old, and the family history was satisfactory. He had had repeated gastro-intestinal disturbance, and had been rather troublesome to bring up. Ten days before admission he was very feverish and vomited. A day or two later there was some discharge from one ear. The fever continued, and he was drowsy and irritable. Four days before admission his left arm and leg seemed weak. On admission his temperature was 100°, pulse 80, respirations 24 per minute, and while the right arm and right leg were moved freely in all directions, the left arm and left leg were held rigid and were continually twitching. In addition, there was a rapid tremor of all limbs and of all the muscles of the body that varied in fineness and rapidity from time to time and was more marked in one part of the body than in another. Over the whole of the left side, face, limbs, and trunk this twitching and tremor were more marked than in the muscles of the right side. There was a spasticity of all the muscles of the body, more marked on the left side than on the right. The deep reflexes were exaggerated on the right side and absent, from spasticity, on the left side. No disturbances of sensation were found. Lumbar puncture gave a clear fluid with 25 cells, mostly lymphocytes, per cubic millimeter, and a slight haze with the Noguchi butyric acid test for globulin. Blood count and ophthalmoscopic and otoscopic examination were negative, and a negative Wassermann reaction was found in both serum and spinal fluid. No tubercle bacilli or other organisms were found in the spinal fluid. The temperature continued to swing from 99° to 101°. Two weeks after admission the spasticity, twitching, and tremors subsided, and on leaving the hospital six weeks later he had entirely recovered, except for a slight tremor of the left foot, and occasionally of the left arm, when he was tired or excited. Since then he has remained well. The character of the tremor, the spasticity and the flexed attitude of the arm and hand, together with the fact that during sleep the affected muscles became quite relaxed, suggested a lesion in the cerebellar-rubrospinal tract. The character of the spinal fluid, the comparatively rapid recovery, and the

occurrence during an epidemic suggested that the polioencephalitis might be due to the same etiological factor as acute epidemic poliomyelitis.

CASE V.—J. C., a boy, aged four years and seven months, with a satisfactory family history and a good previous history, complained of pain in the mouth four days before admission, and his lips were seen to be trembling. The next day he had difficulty in swallowing and seemed feverish, and the following day was unable to articulate or to swallow. On admission his temperature was 102.4° and after reaching 105.4° two days later, settled gradually. He was semicomatose. His face was mask-like, and he lay with head retracted and legs drawn up. The muscles all over the body were rather spastic and there were frequent clonic spasms of the right side of the face, with occasional convulsive twitchings of the arms and legs. On the day after admission the spinal fluid was clear, but contained some small white flakes and 286 cells per cubic millimeter, large mononuclear cells predominating. The cells gradually decreased in number, but the spinal fluid was not noted as normal for two months later. No tubercle bacilli or other organisms were found, and the Wassermann reactions in serum and spinal fluid were at all times negative. Except for a moderate increase in the white blood corpuscles, the examination of the blood was negative. The coma continued for nine days, and then he gradually regained consciousness and the muscular rigidity passed off. The face remained mask-like, and there was a symmetrical weakness of the muscles of facial expression on both sides. The elevators of the lower jaw were nearly completely paralyzed on both sides, the tongue was motionless except for some slight power of elevating the posterior portions, and there was no power of articulation. Saliva dribbled continuously from his mouth, and he could only swallow food when it was placed well back in his pharynx. The orifice of the fauces was wide and cavernous, and the soft palate and pillars of the fauces motionless. The right arm was weaker than the left and somewhat spastic, and showed athetoid movements and incoördination. There were no disturbances of sensation. On leaving the hospital three months later the general condition had improved very much, and the tremors, spasticity, and athetoid movements of the right arm were much less marked. When seen two months later, one side of the soft palate was active while the other was still paralyzed, and four months after that the palate had recovered, and instead of the wide, gaping aperture of the fauces, there was a small aperture with the pillars of the fauces and the soft palate quite mobile. Otherwise, little definite improvement had taken place, though he could swallow better, the saliva dribbled rather less constantly, and he made more intelligible attempts at articulation. Bilateral atrophy of the tongue was noticeable.

PROGNOSIS. Prognosis must always be guarded in the acute stage, as muscles of vital importance may become rapidly paralyzed in the course of a few hours. It is difficult to say when the danger of further spread is over, but although cases are seen where the acute symptoms disappear only to reappear with increased severity after a few days, they are exceptional. When the fever has subsided and appetite and spirits have returned, further spread is unlikely and the prognosis as to life is brighter. A few cases run an acute course, with marked general symptoms that clear up as by crisis in a few days.

CASE VI.—A boy, aged three years and eight months, complained of headache and pain in his chest, and seemed feverish for three days. He appeared to recover, but a day later the same symptoms returned. On the sixth day he was worse and seemed unable to swallow. It was thought that he had diphtheria. On admission on the tenth day of his illness he was emaciated and apparently unconscious, with marked stiffness of the neck and back and a temperature of 102.9° . The spinal fluid was clear and contained 34 cells per cubic millimeter, 95 per cent. of which were mononuclears. The face seemed a little drawn to one side, the voice was feeble, and the tendon reflexes were all exaggerated. Respirations were noisy from the bubbling of the air through the accumulation of mucus in the throat, but no involvement of the respiratory musculature was observed. During the following day the temperature rose to 103.6° , but the condition seemed otherwise the same. On the second day after admission the temperature dropped to 99.8° , and the child could talk and clear his throat, and he was eager for food. A complete paralysis of the left side of the face was the only residual involvement.

Such cases are comparatively rare, and where the acute symptoms pass off gradually it is difficult to prognosticate for some days as to whether further spread will occur or not.

The prognosis as to the ultimate recovery of power in the paralyzed parts is one of still greater difficulty. As a general rule, muscles that show the power to contract at a period when all acute symptoms have cleared up and the child is apparently well except for the paralysis will not become weaker, and can, with careful treatment, regain their power to a variable extent. If the affected muscle be one of a group of similarly functioning muscles, the others of which are active, it is more likely to recover than when all the muscles of the group are completely flaccid. This is well seen in the muscles of the shoulder girdle. The deltoid is more likely to recover if the supraspinatus and infraspinatus are active than when all the scapulohumeral muscles are flaccid. The prognosis also is better for a muscle such as the biceps if the other muscles of the arm are active than when all the muscles of the limb are completely flaccid, and there is probably a destructive

lesion involving the anterior horn cells of the lower cervical and upper dorsal segments of the cord on that side. It is important therefore, that the condition of the muscles at any time be ascertained. It is not sufficient to observe whether or not a muscle is able to perform its function, for a muscular contraction may not be sufficiently strong to move the part, and yet the muscle may not be totally paralyzed. In the legs the tendons of the dorsiflexors of the ankle can often be seen to tighten on tickling the sole of the foot, and yet no movement of foot or toes occurs, and the same stimulus may be sufficient to cause a movement in the muscle mass of the quadriceps extensor that can be felt by a hand placed gently about the thigh, but that cannot be seen or recognized by a movement at the knee-joint. If the knee be bent so that the hamstring tendons are relaxed, and the sole of the foot stimulated, contraction of the hamstrings may be recognized by a tightening of the tendons that is readily felt, although no further flexion of the knee is produced. In a similar way, action of the glutei can be ascertained by pressing with the finger-tip in the region of the gluteal fold or simply by stroking the skin in the same region; of the lumbar muscles by stimulating external to the muscle mass in the angle made by the margin of the muscles and the twelfth rib; of the vertebroscapular muscles by gently stroking the skin internal to the vertebral border of the scapula; of the scapulohumeral muscles by a similar stimulation external to the axillary border of the scapula and over the supraspinous fossa, the arm being placed in a position of partial abduction; of the pectoralis major by stimulating the inner end of the anterior axillary fold with the arm in the semi-abducted position; and of the muscles of the abdominal walls by means of the abdominal and epigastric reflexes. By similar methods of examination, other muscles that appear to be paralyzed are seen to retain some power of contraction or to have regained such power.

With the object of ascertaining whether in the early stages any prognostic value could be placed on the electrical reactions of the paralyzed muscles, 11 cases were tested. With children a general anesthetic is necessary to obtain satisfactory reactions in individual muscles, and this was not considered justifiable, so that complete reactions were not obtained, as the patients soon grew restless and impatient during the examination. It was, however, possible to test one or two muscle groups satisfactorily in the quieter patients, especially in a paralyzed limb, but in no case was it attempted until all tenderness of the acute stage was passed. The earliest to be examined was tested on the tenth day after the onset of paralysis. In this case a weakened quadriceps reacting well to faradism recovered, the calf muscles apparently paralyzed gave a weak reaction to faradism, and at the end of twelve months showed no return of power, and the anterior tibials and peronei gave no contraction to faradic stimulation, and with galvanism, kathodal

closing contraction was greater than anodal closing contraction, ($KCC > ACC$). At the end of twelve months the anterior muscles showed no return of power, but some atrophy. In another case a paralyzed tibialis anticus muscle gave no response to faradic stimulation when examined on the fourteenth day, and with galvanism $ACC > KCC$, but the response was sharp, not sluggish, as in a typical reaction of degeneration. The muscle recovered well in the course of a few weeks. Such a reaction as this was found commonly in muscles that subsequently recovered well. Typical reactions of degeneration with slow response were found in several cases where the muscles subsequently recovered to a varying extent. It is impossible to draw conclusions from the few cases tested, and it is possible that if stronger faradic stimulation had been tried than was possible in unanesthetized patients, contractions to this form of stimulation would have been obtained. It is, however, safe to conclude that muscles giving soon after onset of paralysis no reaction to strong faradic stimulation and giving with galvanic stimulation $ACC > KCC$ may recover.

Even if a muscle is showing commencing atrophy, a partial recovery may take place and the condition of a partially atrophied but active muscle is frequently seen. The question of whether or not the bones of a paralyzed limb will grow in length as the bones of an unaffected limb is difficult to decide without a large number of cases observed over a longer period, but it seems probable that shortening may be expected in a totally flaccid limb, especially in those cases where the muscles of the limb girdle are also completely paralyzed, while no shortening will be found in a limb with only one or two muscles or muscle groups affected. The prognosis is always worse when such muscles as the deltoid and dorsiflexors of the ankle and peronei are affected, as these muscles are more resistant to treatment than any others, and even if all the muscles of a lower limb regain, at least partially, their power, it is likely that the child will always have a limp of greater or less severity. It is impossible to state a period beyond which no further return of power can be expected, especially in cases that have not received careful treatment. In one case that had received vigorous treatment since the onset a muscle thitherto showing no action began to recover at the end of two years, but in a completely paralyzed muscle recovery to any great extent can seldom be expected after a year of unsuccessful treatment.

TREATMENT. For the purposes of treatment, acute poliomyelitis may be divided into three stages: (a) the acute stage of fever and general symptoms, including the period of onset and spread of the paralyzes; (b) the stage of recovery of muscle power; (c) the stage where recovery in muscle power is as complete as it is going to be, and the treatment is applied to the residual condition of deformities, flail-joints, etc. In this last stage the treatment must be surgical,

and will not be dealt with except insofar as indications for such treatment arise in the stage of recovery of muscle power.

(a) Apart from the suggestive work of Netter,⁹ in attempting to control the acute stage by subdural injections of serum from recovered cases, no specific treatment has as yet been discovered that will check the process when it has commenced. When urotropin (hexamethylenamin) is administered by the mouth it may be detected in small quantities in the spinal fluid, and since it was suggested that this might have some power to destroy the virus of poliomyelitis it was hoped that urotropin might check the processes in the central nervous system.¹⁰ Twenty-two cases were treated with urotropin by oral administration. Cases that were still advancing on admission or such cases that showed marked meningitic symptoms were usually treated in this way, and the administration continued only until the acute stage was passed, but in several cases the treatment was continued much longer. Doses of 0.3 gm. three or four times a day were employed in most instances for a child of two years. In one case the administration was continued for four weeks, during which time the patient, a child of three years, had a total of 16.8 gm. In two instances hematuria developed that ceased as soon as the urotropin was discontinued. In a child of two and a half years the hematuria appeared after five days, during which 5 gm. urotropin had been administered, and in a child of one year it developed on the sixth day after the patient had received 6 gm. In no instance did this treatment appear to cut short the acute stage, and in no instance was there any evidence of more satisfactory or more rapid recovery in the paralyzed parts. No decision as to the efficiency of urotropin can be reached without the statistics of a large number of cases, or by means of some precise method of estimating results.

In 1912 Clark,¹¹ published results of the action of intraspinal injections of epinephrin or adrenalin in the treatment of the experimental disease in monkeys during the acute stage, in which the progress of the paralysis was stayed at least temporarily. In 8 cases in which the paralysis was rapidly developing and in which there was extreme respiratory involvement, this line of treatment was tried. The largest dose was 3.0 c.c. of a 1 to 1000 solution injected along with an equal volume of saline and washed in with 1.0 to 2.0 c.c. more of saline, but, as a rule, doses of 1.0 c.c. or 1.5 c.c. were used. There was usually a rise in blood-pressure of from 10 to 20 mm. of Hg. systolic, without any change in the diastolic pressure; the summit of this rise occurred in from twenty to thirty minutes. The increase of pressure disappeared in from

⁹ *Compt. rend. Soc. de biol.*, 1911, lxx, p. 625.

¹⁰ Crowe, *Johns Hopkins Hosp. Bull.*, 1909, xx, p. 102. Flexner and Clark, *Jour. Amer. Med. Assoc.*, 1911, lvi, p. 1750.

¹¹ *Jour. Amer. Med. Assoc.*, 1912, lix, p. 367. The Action of Subdural Injection of Epinephrin in Experimental Poliomyelitis.

forty-five to sixty minutes. The dose was repeated in from three to six hours, and the same rise of blood-pressure was noted. In 3 cases three doses were given. In 1 case, twitchings of the limbs came on a few minutes after each dose, in addition to the rise of blood-pressure. In 2 cases it was thought that the respirations were easier and the diaphragm acting better after the injections, but such improvement was slight and transitory. Of the 8 cases, 5 died, but it is impossible to say that in the 3 cases that lived the cessation of progression in the paralysis was due to the injections.

Except in cases of respiratory involvement where the patient is fighting for breath, the child lies quietly in bed and makes few attempts to move, and complete rest is assured if care is taken to make it comfortable. The twitchings and jerking described above and occasional turning of the head from side to side appear to be involuntary and occur most frequently during sleep or in the drowsy or comatose patients. If care is not taken to obtain a satisfactory posture, however, the child may become very restless. Whenever rigidity, resistance to anterior flexion, or definite retraction of back and neck are present, the child should be supported on its side or a pillow placed beneath the shoulders or back. Pressure on the limbs and trunk should be avoided, where hypersensitiveness of the skin or deeper structures is present, by means of a wire cradle to support the bedclothes or by the clothes being stretched from side to side of a crib, and with a heavy patient a water-bed adds greatly to the comfort. The hypersensitive condition of muscles, tendons, and ligaments makes any position of a limb that results in tension on these structures irksome, and it is found that the position of semiflexion is usually the most satisfactory. If an affected arm be allowed to be at the side, the shoulders and elbows are strained, but comfort may be obtained by means of a pad in the axilla to keep the arm from the side, and the position allows the elbow to be conveniently flexed. A pillow under the knees will in the same way obtain the semiflexed position of the hips and knees, but in most instances the child appears to be quite comfortable with the legs stretched out, and it seems to be in cases of partial involvement of the hamstrings and adductors that the flexed position is desired. The position of the foot is important, and in the majority of cases requires attention. The weight of the bedclothes, on the foot, and in many cases the weight of the foot alone, will cause an extension of the ankle in cases where the anterior tibial muscles and peronei are affected, and if this is allowed to take place for even a few days, shortening of the flexor tendons results and necessitates not only much pain in correcting the position, but has also a deleterious effect on the recovery of the stretched muscles. A light wire or other right-angled splint to support the foot and relieve the tension on the extensor muscles and tendons should be applied, or the foot simply supported in the desired position with

pillows. In the less severe cases that do not remain at complete rest the splint is preferable. In a limb that is not completely flaccid, the muscles, tendons, and ligaments seem readily to become stiff, and no joint should be kept in one position longer than is absolutely necessary. In most cases the pain and tenderness have sufficiently subsided in a few days to allow of gentle handling, and the joints can then be carefully moved. As soon as the acute general symptoms have passed off, the joints should be exercised to their full functional movements and the pain of the stiffened structures must not be mistaken for the pain and tenderness of the acute stage, since the resulting limitation of movement will be the more difficult to correct the longer the delay. If the pain is not relieved by posture, hot applications, aspirin, or opium preparations may be necessary.

The general treatment during this stage is similar to that of any acute infection. In the severe and possibly fatal cases with the respiratory involvement, diffusible stimulants were administered, and when the dyspnea became marked, oxygen was administered without any lasting benefit. Artificial respiration has been attempted when the respiratory musculature failed rapidly, but in all cases the heart failed before any return of power in the respiratory muscles appeared.

Defecation is sometimes difficult to regulate, and this is seen in cases that have weakness of the muscles of the abdominal wall, and also in cases that show no apparent impairment of the voluntary muscles concerned. Large doses of cascara, castor oil, or calomel, and saline purgatives have frequently to be followed by enemas before evacuation is obtained. Similar difficulty with micturition is seen, and catheterization may be necessary, but does not often continue for more than a few days.

Little trouble is experienced with diet. During the early days the patient will not eat solid food, but is thirsty and will take sufficient milk. As soon as the general symptoms pass off, the appetite returns and there is no indication for restricting the diet. A few cases require to be fed with a nasal tube because of the paralysis of the pharyngeal muscles, and cases where the tongue or palate is involved, require the care that similar conditions in other diseases necessitate.

In spite of careful treatment, cases with impairment of the muscles of respiration or of the upper respiratory passages may develop an inflammatory condition of the lungs that results in a fatal termination, without further spread of paralysis.

(b) The treatment during the second stage of recovery and return of muscle power must be based on the pathology of the condition so far as that can be ascertained. The acute inflammatory action is at an end, the edema is probably disappearing, the cells that will not recover are being absorbed, and those that are less severely

damaged are perhaps slowly recovering. The centres supplying certain muscles or muscle groups may be entirely destroyed, while in other centres most or only a few of the anterior horn cells are intact, sufficient, perhaps, to give the muscle power of voluntary contraction or sufficient, perhaps, to contract a small portion of the muscle or give the whole a feeble stimulus, but at first unable to cause the muscle to functionate in a recognizable manner. Every stage is seen between muscles that spontaneously recover in a few days and muscles that will never regain their power. No treatment is known that can hasten the resolution process in the central nervous system, and the muscles must, therefore, be maintained in a condition as satisfactory as possible as regards nutrition, and their control by means of the central nervous system must be encouraged. Their nutrition can be most efficiently maintained by vigorous massage and by other measures, such as hot air or water-baths that stimulate the circulation in the part. The central control can probably be encouraged most efficiently by the voluntary effort to cause the muscle to contract—that is to say, by active exercises. That electrical treatment by galvanic current can do more than act as massage is doubtful, and when the faradic current can cause contraction it would appear to be only a form of involuntary exercise due to stimuli at a point distal to the anterior horn cells, from which the voluntary stimulus is to arise. Electrical treatment may be a useful adjunct to massage and exercises, but cannot replace them. The use of high-frequency currents has been advocated,¹² even in the earliest stage, in the belief that it causes a diminution of the edema in the spinal cord, but satisfactory demonstration of its efficiency is lacking.

As soon as the acute process has subsided massage must be commenced. At first it can only be gentle and for a short period, but as the nurse or attendant gains the confidence of the child, the treatment may be increased in vigor until deep kneading of the muscle masses for twenty or thirty minutes two or three times a day can be borne. Passive movements must be performed at all the joints to prevent any limitation of movement, and it is found that if these are properly carried out from the beginning there is only in exceptional circumstances any troublesome contractures. There is danger in too vigorous application of such movements, which may stretch capsular structures and loosen joints, such as the knee or the shoulder. The active exercises must depend upon the age of the child and are most successful in the very young patients if regarded as play. A patient of less than two or three years cannot be taught to perform systematic movements, but can be stimulated to perform these movements in play. Floating toys in a warm bath provide the necessary stimulus, and the water

¹² Frauenthal, H. W., Jour. Amer. Med. Assoc., 1913, lxi, p. 2219.

gives a useful support to weakened limbs. A ball or a bright object may be used to encourage movements of an upper limb, and similar tricks may be devised for the lower limbs. The dispositions of the patients are very variable and no two children can be treated alike. Even if no movements of the limbs are seen, the stimulus must be applied and the child helped in the movements at first. The more the child tries, the more successful the treatment. With a child of over three years the intelligence is such that more systematic movements can be employed. Definite exercises against resistance must be detailed for each muscle or muscle group affected.¹³ The weight of the limb may be sufficient resistance at first or it may be too great and help must be given, or it may be too little and gradually increasing pressure against the movement must be employed. Even though no movement is effected it must in all cases be attempted. After the muscles have been loosened and warmed by massage is the best time for the exercises. Before the muscle is strong enough to raise the part, a good method is to raise it passively and then allow the limb to fall slowly by its own weight, telling the child to prevent it from falling. In this way contractions of muscles can early be made effective. The spastic and ataxic conditions occasionally met with should be treated just as the flaccid condition by massage and movements passive and active.

While the muscles of a limb are recovering they regain their power at different rates, and in the majority of cases are not equally paralyzed at the commencement of the recovery, so that it frequently occurs that one muscle is capable of strong contraction while the antagonizing muscle or muscle group is still feeble. Contractures of the stronger muscles and tendons and stretching of the weaker will result, and this may tend to deformities that require operative interference if not corrected early. Stretched muscles do not recover as readily as relaxed muscles, and it is therefore important to be on the watch for such conditions and to prevent the stretching and contractures. Passive movements may be sufficient if the difference in the strengths of the muscles is not great. Splints are frequently necessary. This is well seen in the case of the ankle. When the muscles of the leg are completely flaccid the weight of the foot is sufficient to cause severe drop, but if the calf muscles are active the drop will be more difficult to prevent. The foot must therefore be fixed in the position of dorsiflexion by means of a light wire or other posterior right-angled splint or by strapping with adhesive plaster as employed by Herrick.¹⁴ It may be sufficient to have it fixed during the night only, and free to move and exercise during the day, or it may be necessary to keep it fixed day and night, the splint being removed only when

¹³ Wright, Boston Med. and Surg. Jour., October 24, 1912. Muscle Training in the Treatment of Poliomyelitis.

¹⁴ New York Academy of Medicine, Surgical Section, March, 1914. (Not yet published.)

massage is to be given and the part exercised. A plaster cast or other splint that cannot be removed for treatment is to be avoided. In any situation where weakened muscles are liable to be stretched the position of the limb should be altered and maintained by suitable support. The deltoid is peculiarly situated, in that the arrangement of the origin and insertion necessitates a considerable power of contraction to raise the weight of the limb. A degree of weakness that would allow of functional movement in another muscle will give the effect of a total paralysis in the deltoid, and the return of power must be considerable in the deltoid before the abduction of the arm can be effected. The arm hangs by the side and the deltoid is kept on the stretch, a condition inimical to recovery. It is difficult to obtain the support necessary short of surgical interference such as that employed by Bartow.¹⁵ A light splint made of poroplastic, moulded to the chest, axilla, and upper arm, is effective in many cases. Supporting the arm by means of such a splint in the position of partial abduction relieves the muscle and places it in a position more advantageous for functional movement, but is unsatisfactory in that it does not relieve the drag on the capsule of the joint. Care must be taken that with active adductors and stretched capsule and deltoid the splint does not act as a fulcrum to force the head of the bone from the glenoid cavity and still further stretch the weakened structures. While the patient is still in bed, a soft pad in the axilla is sufficient support.

Attention has frequently been drawn to the crippling results of paralysis of the deltoid muscle and to the small extent to which recovery takes place in the case of this muscle. In 30 of our cases, one or both deltoids were noted as paralyzed completely or partially. In 16 cases the condition was bilateral and in 14 one or the other muscle only was affected, and of the forty-six muscles affected, thirty-six were noted as completely paralyzed; 9 of the 30 cases died during the acute stages or were lost for observation immediately after, and of the remaining 21 cases there were 28 deltoids available for observation. Of these twenty-eight deltoids that were observed for three or four months after the onset, 15 were carefully supported from the first, and of those two only showed no improvement at the end of that period, while of the thirteen unsupported muscles, five showed no improvement at the end of the same period.

Weakness of the extensors of the ankle and the resulting drop-foot is as difficult to affect by treatment as weakness of the deltoid, and is a source of trouble not only in the disability it causes, but also that the leg is swung out and externally rotated when the child walks, to avoid the drag of the toes. This may cause tilting of the pelvis and lateral curvature of the lumbar region of the spinal column. Ambulant braces will correct the drop, but are often so

¹⁵ Shoulder and Arm Paralysis of Poliomyelitis, New York Med. Jour., 1913, xcvii.

heavy that the weakened limb swings as before, and the tilting and curvature again result. The question of braces is one of much practical difficulty. If a child can walk without deformities resulting from the weight of the body acting on a weakened limb, a brace is unnecessary. If the patient is unable to support the body weight properly, without causing deformities, he should be kept off his feet as much as possible, and by means of massage and exercises against resistance the muscles should be encouraged to regain their power. The muscles will continue to improve for two or three years at least. In many cases a child cannot and should not be prevented from walking before the legs are strong enough to maintain the body weight without deformities resulting, and then some support is necessary for the joint or joints involved. The heavy ambulant braces usually applied are often unnecessarily extensive, and their weight is extremely hampering, and instead of being applied only when the child walks, they are kept on constantly so that the exercises necessary for the development of the power in the muscles are impossible, and the ultimate result is not so good.

When a child with lower limbs affected has so far recovered that they can support the body weight satisfactorily, but walking is hampered because of the foot-drop, an elastic strap from the dorsum of the shoe and fixed below the knee to a garter or to some convenient garment is sufficient to support the ankle and allows of the leg being moved forward without the swinging and tilting movement. In many cases faulty movements, such as external rotation of the thigh, are developed in the earlier attempts at walking, probably because of excessive action of the external rotators over the gluteus medius and gluteus minimus and other muscles that cause internal rotation. If care is taken during the further recovery to direct the child's attention to this fault and to urge it to swing the foot straight, the tendency to external rotation as an accompaniment of flexion disappears. The older the child the more its efforts can be utilized and directed toward a satisfactory prevention of deformities and faulty movements, and it is in the early stages of recovery that such directed effort will be most efficacious. Striking contrasts are seen between the results obtained when the mother or attendant appreciates the requirements and when the directions are carried out without proper understanding of these requirements.

The muscles of limbs and trunks can be treated effectively by massage and exercises, but those of the face, pharynx, tongue, etc., can only with difficulty be reached by such methods. These muscles, however, are so situated that they are being continually exercised and massaged by the movements of the neighboring parts, and they are continually receiving stimuli for active movements, so that further treatment seems unnecessary. The muscles of the face are amenable to electric treatment, and though it is difficult

to draw conclusions as to the relative efficacy of treatment, cases treated electrically do not appear to recover more rapidly than those that are let alone. Because of the fact that cases are seen showing every stage in rapidity of recovery from the muscle that regains power in a day to the muscle that regains no power and progressively atrophies, it is peculiarly difficult to judge of what effect, if any, the treatment has had, the more so since muscles that for months show no voluntary movement and commencing atrophy will even then commence to recover in cases that have received no treatment. No two series of cases are quite comparable, since epidemics vary in severity not only as to fatality, but as to localization and severity of paralysis. Treatment must, therefore, be directed along lines that follow the indications of the pathology of the disease and that are most likely to prevent crippling and deformities. The conditions vary in each case, but by following the indications to maintain the nutrition of the muscles, to encourage movement and to prevent deformities, and by carrying out such treatment energetically, carefully and logically, much of the crippling effects of the disease can be prevented.

GALL-STONES VIEWED FROM A SURGICAL STANDPOINT.

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IN considering the subject of gall-stones from a surgical standpoint, we are concerned equally with the internist in the consideration of the etiology, inasmuch as the conditions which determine their origin must likewise be important factors in their recurrence after operation. Until recently the dictum of Naunyn has been accepted, namely, that with stasis of the bile in the gall-bladder there occurs an infective inflammation of its lining membrane, and under these conditions only does the precipitation of cholesterin take place. A notable contribution to our knowledge on this subject is the work on cholelithiasis by Aschoff and Baumeister. Therein it appears that the solitary gall-stone has a different composition than have multiple gall-stones. The former is composed of pure cholesterin, usually with a nucleus of pigment. The cholesterin is arranged in radiating rods. There is no lamination. This form of stone is found in non-infected gall-bladders, and arises therefore without preëxisting inflammation. The multiple stones are laminated and are of mixed character, containing cholesterin, lime salts, and pigment. These are always the result of an infective

process. However, the pure cholesterol stone may provoke sufficient irritation in the gall-bladder to subsequently arouse an infective inflammatory process, and resulting therefrom multiple stones may form. Whatever may be the explanation, women are much more susceptible to gall-stone disease than men. The pressure of their clothing and pregnancy are by some considered responsible, while the character of food and constipation are regarded as etiological factors. Aschoff and Bacmeister hold that dropsy of the gall-bladder always depends upon a previous inflammatory process. Their work is based upon the thorough pathological examination of 250 gall-bladders which had been excised because of the inflammatory changes in them. Fifty other gall-bladders removed from dead bodies were likewise subjected to their careful investigation.

In determining the source of infection of the gall-bladder, investigation has proved that it may be either of ascending or descending character. The organisms are those usually found under normal conditions in the intestinal tract. Thirteen minutes after Kraus made an intravenous injection of bacteria, he was able to demonstrate their presence in the hepatic duct. It is well known that in the early stages of typhoid fever the bacilli are present in the blood. These bacilli may find their way into the bile through the bloodstream or may enter the bile-current through the excretory function of the liver, or they may ascend from the intestines through the common duct and thus find their way into the gall-bladder. Other infective processes, like pneumonia, influenza, and erysipelas, have been known to provoke cholecystitis. Naunyn injected virulent bacteria into a normal gall-bladder where their motility was nowise disturbed, and they disappeared after a short time.

Gall-stones can provoke infection of the gall-bladder in various ways: (1) the mucous membrane may be lacerated by a stone; (2) a stone may by pressure interfere with the circulation; (3) the obstruction may cause stasis of bile; (4) bacteria may be present in the gall-stones.

Cancer of the gall-bladder was found by Aschoff and Bacmeister in 9 cases. Of these 2 presented radiating stones. Evidently in these the stone was primary and the malignant process secondary. In 5 the stones were multiple and of the mixed type. In these it was impossible to determine whether the cancerous invasion was primary or secondary. In 2 cases of cancer of the gall-bladder no stones were found.

Körte in discussing the relation of cancer to gall-stones established three groups of cases. The first included patients who for years had symptoms of gall-stones which finally merged into those suggestive of cancer. In the second group he placed those who having had symptoms of gall-stones, presented a long period of quiescence, after which came the manifestations of cancer. In the third group there had been no previous symptoms of gall-

stones whatsoever. Of the 32 cases, 14 belonged to the first, 10 to the second, and 8 to the third group.

Referring again to infective processes which may involve the gall-bladder, it should be emphasized that cholecystitis may occur without the presence of gall-stones. It may be an acute complication of typhoid fever. However, its occurrence as a sequel of typhoid fever does not necessarily establish a causal relationship. In a case of cholecystitis, which occurred a month after the termination of an attack of typhoid fever, presenting the usual acute abdominal symptoms—namely, pain referred to the right hypochondrium, marked tenderness, localized rigidity, and the presence of a tumor, but without biliary colic—at operation an inflamed gall-bladder was found greatly distended and adherent to the pyloric end of the stomach. The inflammatory contents contained the pneumococcus, but no typhoid bacilli.

While gall-stones are ordinarily formed in the gall-bladder, they may originate in the biliary route. According to Adami, gall-stones are most frequently found in the gall-bladder, next in the cystic, then the common duct, and least frequently in the hepatic duct.

With an infective process established in the gall-bladder, various changes can occur. The gall-bladder may become greatly distended. In one of my cases it reached well below the level of the umbilicus and contained over a quart of fluid. The virulence of the infection may destroy the lining membrane and even lead to gangrene and perforation of the gall-bladder with localized or general peritonitis. The infectious process may spread to the surrounding structures and produce marked adhesions to the pylorus and duodenum. Sometimes the adhesions serve as a protection so that a perforation of the gall-bladder into the duodenum can result. An opening of sufficient size may be established to permit the passage of gall-stones directly into the duodenum and cause intestinal obstruction. These stones usually pass down to the lower part of the ileum and become fixed at or within a few inches of the ileocecal valve. A mass of such dense hardness is found that it suggests carcinoma. The clinical picture of chronic intestinal obstruction is presented. Many times no preceding manifestations had occurred to arouse a suspicion of gall-stone disease, and the finding therefore has been entirely unexpected.

Mixed infections occur at times, causing hemorrhagic septicemia. Twice the writer has seen the body covered with purpuric areas, and even extensive ecchymosis, each time in advanced and neglected cases of gall-stone disease. The tendency to hemorrhage in cases of persistent jaundice is too well known to require more than reference to it.

Adhesion to the peritoneum and to the structures mentioned may lead to distortion of the gall-bladder and kinking of it. In conse-

quence there may be sufficient interference with the passage of bile to cause biliary colic. It is because of these adhesions that patients frequently suffer after gall-bladder operations, the suffering assuming the same type and the symptoms being of the same kind as when they had true gall-stone colic.

The varying pathological conditions with which the surgeon has to deal explains the incongruity of the clinical picture. The most frequent symptom of gall-stone disease is biliary colic. Its production depends upon the free admission of bile into the gall-bladder and the temporary interruption of its discharge into the common duct because of the presence of a stone or other obstruction. If the gall-bladder becomes entirely filled with gall-stones, bile sand, or a putty- or clay-like material, so that these substances are fixed within its cavity, the patient may never experience biliary colic.

The gall-bladder normally does not hold more than an ounce of fluid. Mayo has pointed out, therefore, that it cannot serve as an organ of storage. As there is secreted each day from thirty to fifty ounces of bile, the capacity of the gall-bladder is utterly insufficient to serve such a purpose. Evidently, therefore, its function is to relieve the tension upon the common and hepatic ducts as well as of those which lead to the pancreas. It likewise secretes a quantity of mucus which has a definite physiological purpose in serving to reduce the probability of occurrence of pancreatitis or other complications. When more or less complete obstruction in the cystic duct occurs, and the contents of the gall-bladder fail to find an outlet, the fluids within this sac become absorbed and the gall-bladder contracted. In the end we frequently find it so small, and when packed full of stones so hard and dense, that it can only be a source of irritation. The opening of the pancreatic ducts at the ampulla of Vater favors the extension of the infectious process to the pancreas, and hence subacute or chronic pancreatitis is a frequent complication of gall-stone disease. The appreciation of its occurrence is essential in determining the indications for surgical operation.

In a recent paper by W. J. Mayo, based upon his experience and that of his associates, in which he reviews 4000 operations on the gall-bladder and biliary passages, he reaches the conclusion that the mortality associated with this condition is due to the complications incident to the disease and resulting from delay rather than the removal of the gall-stones. He shows very clearly that the death rate is greatly increased when the disease has been allowed to advance until the deeper biliary passages, liver, pancreas, and the neighboring viscera become involved in infectious processes or adhesions. On the other hand, the early removal of gall-stones from a gall-bladder not otherwise affected is an innocent and simple operative procedure. The surgeon has been taught by experience that the incision and drainage of the gall-bladder is, generally

speaking, a wiser step than is the excision of the organ. The particular reason for this is that not only can the gall-bladder be preserved and serve the function for which it was intended, but that continued drainage leads to a cure of the diseased condition which may exist in the pancreas and removes infection from the biliary passages.

As much of the disturbance which has followed operations on the gall-bladder has been due to traction of adhesions, kinking of the gall-bladder, or biliary channels, it is wise in establishing the drainage to guard against fixed adhesions. Although it has been proved that a gall-bladder fastened to the peritoneum, if it does not produce marked traction or kinking, does not lead to the reproduction of gall-stones, the tendency of recent years has been to drain the gall-bladder without anchoring it. Nearly all of the suffering which occurs after gall-bladder operations, which is frequently taken for a recurrence of the gall-stones, is due to these adhesions and the consequent displacement of the biliary channels. That these conditions can occur without the presence of gall-stones is evidenced by the fact that we frequently encounter patients who have apparently suffered from cholelithiasis, but upon opening the gall-bladder we find either an hour-glass constriction of the gall-bladder or adhesions about this structure and no gall-stones. Recently I operated upon a patient who had passed gall-stones freely for a number of years. The gall-bladder was in a state of chronic inflammation, and had numerous diverticula, but a careful search did not discover a single gall-stone. All of the manifestations evidently had been kept up by the adhesions.

The frequent association of disease of the gall-bladder and the appendix is known to all surgeons. Gall-stones may remain latent and may not have provoked any manifestations until an infectious process in the appendix or elsewhere in the abdomen has awakened a secondary infection in the gall-bladder. This should not surprise us when we remember that only a small percentage of the people having gall-stones suffer therefrom. Autopsy reports show that 10 per cent. of all bodies present gall-stones, and of this large number 95 per cent. never had any manifestations suggesting the presence of gall-stones during life. The surgeon today, therefore, examines the gall-bladder as a matter of routine in every opened abdomen.

A movable kidney can be responsible for the symptoms of gall-bladder disease. Treves has reported cases in which a movable kidney has produced pressure upon the cystic duct interfering with the passage of bile from the gall-bladder and provoking symptoms of biliary colic which were relieved by fixation of the kidney. On the other hand a movable kidney may become fixed at the site of the gall-bladder, and if it become infected may strikingly resemble cholecystitis. This was illustrated in a case presented at the writer's clinic a number of years ago, in which the patient had been

acutely sick for a few days. Her temperature was above 104° at the time of her admission. She had a large tender tumor in the right hypochondrium, reaching down to the umbilicus, which was tense, fluctuated, and occupied the normal position of the gall-bladder. With an aspirating needle pus was withdrawn. Upon opening the pus sac it was found to be made up of a series of compartments, and was recognized as a pyonephrosis. After the infectious process had subsided a urinary fistula formed which persisted for some time. Similar cases have been reported by other surgeons.

We can best illustrate the points we desire to emphasize by presenting briefly the histories of a few cases taken from our clinical records.

CASE I.—A typical case of single gall-stone producing obstruction to the outflow of bile and resulting in cholecystitis.

The patient was a woman, aged forty-three years, seen in consultation with Dr. Sears, December, 1902. Eight years previously, while a patient at Mt. Sinai Hospital, she was told that she had gall-stone disease. An operation was advised, but was declined. For the five months preceding my consultation, the patient, having been free from manifestations for a number of years, had recurring attacks of pain, each lasting from several days to a week. These would begin in the epigastrium and extend to her back. She was admitted into St. Joseph's Hospital, February 28, 1903, at which time an elastic tumor could be felt in the right hypochondrium, which apparently could be moved laterally and was moderately tender. There was slight rigidity of the upper portion of the right rectus muscle. On March 2 I operated upon her at my clinic and found a single gall-stone about an inch in length and three-quarters of an inch in width. The tumor which we had been able to palpate proved to be a Riedel's lobe of the liver. The gall-bladder presented extensive adhesions. The patient made an uninterrupted recovery, and now after ten years has had no recurrence of the trouble. This case is typical of the disturbance caused by a single movable stone associated with a mildly infectious cholecystitis.

CASE II.—Gall-stone impacted in the gall-bladder at its cystic end, producing acute gangrenous cholecystitis.

The patient, a woman, aged forty-three years, was seen at her home in Elbridge, November 3, 1907, with Dr. Kaple. Prior to that illness she had experienced attacks of severe abdominal pain without fever which would last never longer than a day. Five days before she was seized with general abdominal pain, which became fixed in the right side. Her temperature ranged from 99.5° to 101° . At the time of my examination the pulse was 100, temperature 101° , and there was leukocytosis of 33,000. Tenderness was present in the right upper quadrant of the abdomen, where there was also an increased area of dullness which reached almost to the level of the umbilicus. There was marked rigidity, but no jaundice.

An incision was made through the right rectus, and ptosis of the liver was found. The gall-bladder was dark, swollen, and tense. Upon incision a gall-stone an inch and a half long was found wedged into the cystic duct. The entire mucous lining of the gall-bladder was gangrenous, and was easily removed. The gall-bladder was drained. The patient made an uneventful recovery.

CASE III.—*Gall-stones with cholecystitis, causing frequent and acute exacerbations for a number of years; operation deferred until the occurrence of rupture of the gall-bladder.*

The patient was seen first by me March 20, 1904, with Dr. Levy. The attacks of gall-stones colic had been characteristic. On one occasion there had been associated jaundice. The pain had each time been very severe. In different attacks he had been seen by various physicians, all of whom had concurred in the diagnosis and had recommended operation. Early in 1905, after a severe attack he agreed to go to the hospital, but he failed to report for operation. On December 15, 1906, he became prostrated with the most severe attack he ever had had. Three days later he was admitted to St. Joseph's Hospital. At that time he had a pulse of 120, temperature 102°, and was jaundiced. The abdomen was distended and generally rigid. Because of the evident general peritonitis, operation was deferred, with the hope that under rest, the exclusion of fluids, and the administration of the Murphy drip the infection might become localized. The urine contained both albumin and casts. The temperature began to subside and the rigidity and dullness were restricted to the right hypochondrium; but he grew so nervous and seemed to be possessed of such fear of an operation that he was unable to sleep or to control himself. On December 26 I operated upon him. The omentum was adherent to the liver and the intestines. The gall-bladder had been ruptured. The exposed area was occupied by structures which had become matted together by the infectious process. One large space was found which contained a quantity of bile, and in this way the lower border of the liver was finally found, and what remained of the gall-bladder was seen. It was a gangrenous mass, and thick yellow bile was pouring out of it. A rubber drainage tube was introduced and the area packed off with gauze. The patient's condition on the table was not satisfactory. He rallied and seemed better later in the day, but the improvement was only temporary. The urine became entirely suppressed. The temperature rose to 105°. He had a series of severe convulsions, and died about forty hours after the operation.

CASE IV.—*Gall-stones after causing repeated attacks of biliary colic became latent for ten years, when acute cholecystitis developed as a complication of typhoid fever.*

The patient, a woman aged thirty-four years, was seen at her home in Oswego in consultation with Drs. Elsner and Eddy, November 7, 1904. Up to ten years previously she had had repeated attacks

of biliary colic, but none again until her present sickness. She was in the third week of an attack of typhoid fever, when she was seized with a chill and severe pain in the right hypochondrium. Dr. Elsner was called to see her and found a large tender mass in the right upper quadrant of the abdomen. During the night a quantity of gritty bile sand was discharged per rectum. There was a slight reduction in the size of the mass and moderation of tenderness. Jaundice was present. The urine contained a trace of sugar. At the operation the omentum was found adherent to the gall-bladder. Four ounces of fluid were withdrawn from this sac. The first of it was watery and the latter portion purulent. The gall-bladder was opened. Fifteen gall-stones were removed, of which eight were large. No bile sand was found. The gall-bladder was drained. The patient made an uneventful recovery, and has remained well since.

CASE V.—*Gall-stones causing cholecystitis, chronic pancreatitis, and toxic nephritis.*

A woman, aged thirty years, married but never pregnant, had her first attack of gall-stone colic six years previously. She was referred to me November 21, 1906. At that time she had been suffering from an attack which had been of five weeks' duration. The pain had been constant. She had no fever. She had persistent jaundice. There was tenderness over the gall-bladder, but no definite tumor. The urine was dark, sharply acid, had a specific gravity of 1032, contained 2 per cent. of albumin, $2\frac{1}{2}$ per cent. of sugar, and hayline and granular casts. Dr. Coon made three exposures for the purpose of taking x-ray pictures. Disturbance in the region of the gall-bladder was indicated in these plates, but a definite diagnosis could not be made therefrom. At the operation the gall-bladder was found adherent to the surrounding structures, and the adhesions were too dense to be separated. A single stone was found in the gall-bladder. The pancreas was hard and dense. Drainage was continued for three weeks, at which time the urine had become free from albumin and sugar and the granular casts had disappeared. The patient made a complete recovery, and has remained well since.

CASE VI.—*Gall-bladder filled with inspissated bile, bile clay, and gall-stones without causing any manifestations until within ten days of operation, when acute cholecystitis developed.*

A woman, aged fifty years, was sent to St. Joseph's Hospital, September 20, 1903, by Dr. McKenna. She had suffered from frequent and severe headaches, but had had no particular abdominal discomfort until a week prior to the date of her admission. She attributed her gastric distress to indiscretion in diet. For five days she had had increasing abdominal pain. She complained of difficult breathing. The pain was constant, not of colicky character, and was referred to the right side of the abdomen above the level of the umbilicus. On admission her pulse was 96, temperature 100.6°.

There was an apparent prominence to the right of the median line, midway between the umbilicus and the ribs, about the size of a small orange. It was tense and tender, and could be moved from right to left. She had been given a dose of castor oil the night before, and the bowels moved freely. The stools were watery. During the next forty-eight hours the temperature remained stationary, namely, about 100.5° , but the mass increased steadily in size, and rigidity of the overlying muscles became apparent. The blood examination showed 68 per cent. of hemoglobin, 3,800,000 red cells, and a leukocytosis of 19,000. On opening the abdomen, September 23, namely, ten days after the first manifestations, the tumor was found to be a distended gall-bladder presenting a plastic exudate, which made it particularly adherent to the liver. Upon incising the gall-bladder, several ounces of a thick mucoid substance were discharged. The gall-bladder was filled with a grumous substance, which was firmly packed in it, but was washed out by means of a stream of sterile water. This material was like soft clay, and embedded in it were twenty-eight stones. No other involvement of the biliary tract was apparent. Drainage was introduced. The patient made a satisfactory recovery, and has remained well since.

CASE VII.—*Gall-bladder and cystic and common ducts filled with gall-stones and clay, never having caused biliary colic; jaundice persistent for seven weeks prior to operation.*

This patient, a Catholic priest under the care of Drs. Muench and Larkin, was referred to me December 28, 1911. He was forty years of age. For a number of years he had suffered from indigestion. During the previous summer, gastric distress was marked. At no time was there characteristic biliary colic. A day or two after his admission into the hospital he developed jaundice. Upon exposing the gall-bladder it was found to be contracted. It was filled with gall-stones that were set firmly in the biliary clay. There was no fluid in the gall-bladder. The cystic and common ducts were equally impacted. The gall-bladder was fixed by adhesions too firm and dense to be separated. Sixty-eight stones were removed, as well as a large quantity of clay. The greatest difficulty was experienced in clearing out the common duct. Despite the jaundice, the hemorrhage at the operation was trivial. Drainage of both the gall-bladder and common duct was established. Uninterrupted recovery and complete restoration to health followed.

CASE VIII.—*Gall-stones; cholecystitis; thirty-three stones removed from the gall-bladder; one embedded in the cystic duct likewise removed; prompt healing of the wound; early recurrence of the manifestations; second operation performed four months later and a stone found in the common duct; choledochotomy.*

The patient, a woman, aged forty-eight years, had suffered from recurring attacks of pain in the region of the gall-bladder extending

to her right shoulder. The more recent attacks had been associated with jaundice, clay-colored stools, and dark urine. There was increased rigidity over the upper half of the right rectus and a moderate area of dullness. She was referred to me by Dr. Elsner, and operated February 10, 1903, at the Syracuse Hospital for Women and Children. Upon exposing the gall-bladder it was found embedded in a mass of adhesions. Two drams of light-colored serum were withdrawn. No free bile was found in the gall-bladder. Thirty-three stones were removed from the gall-bladder and one which was impacted in the cystic duct. Upon its removal the bile flowing freely. At this time the common duct was examined and no stone found in it. Soon after leaving the hospital she began to have a recurrence of manifestations. There was pain associated with jaundice. Albuminuria was present. The bowel movements had normal color. On June 17, 1903, I operated upon her again; this time at the City Hospital of Watertown. No stones were found in the gall-bladder or the cystic duct, but one was discovered in the common duct near the duodenum. The duct was incised and the stone removed. She suffered from cholangitis following the operation, but despite this condition made a recovery, and has remained well since.

CASE IX.—*Gall-stones embedded in a contracted gall-bladder; cholecystectomy.*

On February 8, 1909, a man, aged forty years, who two years previously had been under the treatment of Dr. Heffron for chronic diarrhea and colitis, gave a history of having had for two and a half years attacks of pain in the right upper quadrant of the abdomen, which recurred every three months. With some of these attacks he became jaundiced. On physical examination a tumor was found at the site of the gall-bladder extending almost to the level of the umbilicus. It was tense and hard. There was still associated colitis. He was operated upon February 19, 1909. The presenting tumor was found to be a Riedel's lobe of the liver. Beneath it was a small hard gall-bladder containing no fluid. The gall-stones filled its entire lumen. The cystic duct was clamped and the gall-bladder stripped out without opening into it. The man made an uneventful recovery.

CASE X.—*Gall-stones in the gall-bladder, and cystic and common ducts; persistent jaundice; extensive hemorrhagic areas upon the surface of the body; uncontrollable hemorrhage following operation; fatal ending.*

Patient, aged fifty-nine years, was brought to me May 16, 1905. Fifteen years before she had had what was called bilious fever. Five years before she had suffered from neurasthenia, which was characterized by great weakness, dizziness, pain in the head and neck, sensitiveness of the spine, and inability to do the ordinary housework required of her in her home. When her last illness

began ten weeks prior to her consulting me she complained of aching and tenderness of the dorsal spine, inability to concentrate her mind upon the work she had been accustomed to do daily. Soon after this time she had intermittent abdominal pains, which were thought to be due to indigestion. Later still the abdominal pain grew more severe, making sleep impossible. There was no vomiting. Gradually deepening jaundice appeared. For eight weeks she had been profoundly jaundiced. During this period she suffered from itching of the skin, an irritating cough, excessive nervousness, nausea, and intestinal fermentation. She had to be brought to the hospital a long distance on a cot. On admission a number of large ecchymotic spots were found on her thighs and buttocks. In the right hypochondrium was a mass which extended to the level of the umbilicus. It was about five inches in its transverse diameter. Her temperature was 99°; pulse, 80. Upon exposing the abdomen the mass was found to be a Riedel's lobe almost purple in color. The liver was turned up and the presenting gall-bladder was yellowish in color and about ready to rupture. Upon aspiration five ounces of pus were withdrawn. A large number of gall-stones were removed. Some were also removed from the cystic duct, while the common duct was found to be thickened. There was reason for suspecting that this thickening might be malignant. A flexible probe was carried through the duct into the duodenum. At the operation there was little bleeding. She had been given chloride of lime before the operation, and this was continued per rectum subsequently. On the day following operation the dressings were found stained with blood. A clot of considerable size was found about the tube which drained the gall-bladder. The bowel movements were darkly colored. Uncontrollable oozing, which developed into quite free bleeding, occurred. Adrenalin, strychnine, and chloride of iron as well as chloride of lime were administered. Suppression of urine followed. There never was a rise of temperature. Persistent vomiting appeared. The patient died on the third day after operation.

1. CONCLUSIONS. Gall-stones can exist through life without provoking any manifestations.

2. Single gall-stones form frequently without infection.

3. Multiple gall-stones are usually dependent upon a preëxisting cholecystitis.

4. The typhoid bacillus, the pneumococcus or the streptococcus can awaken acute cholecystitis in a gall-bladder containing stones.

5. Gall-stones can by traumatism, pressure, or interference with the biliary current cause cholecystitis.

6. As a result of inflammation of the gall-bladder, adhesions form, distorting the biliary route and changing the normal configuration of the gall-bladder.

7. Perforation of the gall-bladder may occur, causing localized or general peritonitis.

8. Through the perforation, a gall-stone may pass of sufficient size to cause intestinal obstruction.

9. Cancer of the gall-bladder may be a sequel of gall-stones.

10. As a result of infection hemorrhagic septicemia may occur, or because of the persistent jaundice, hemorrhages may arise or the character of the blood may become so altered as to interfere with its coagulation.

11. Gall-stones are not harmless tenants of the body.

12. With the definite evidence of their presence, surgical attention is required.

13. Early operations are attended with little danger, and the removal of gall-stones from a bladder followed by drainage promises permanent relief.

14. Neglected cases yield poor results, and fatal termination follows operations performed at the eleventh hour.

A CRITICAL STUDY OF LANGE'S COLLOIDAL GOLD REACTION IN CEREBROSPINAL FLUID.

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LANGE,¹ in 1912, described the action of cerebrospinal fluid in various conditions upon a colloidal gold solution. He demonstrated that the reaction could be used as a delicate test, differentiating normal from pathological cerebrospinal fluids, and more particularly syphilitic from other affections of the central nervous system. Zaloziecki,² Jaeger and Goldstein,³ Grulee and Moody,⁴ and Eicke⁵ have confirmed the value of the test.

The theory of the reaction is based upon the following observations made by Zsigmondy in the course of this study on metallic colloidal solutions.

1. Solutions of electrolytes precipitate colloidal gold.

2. Proteins in the absence of an electrolyte also precipitate a solution of colloidal gold.

¹ Berl. klin. Woch., 1912, No. 19, p. 897; Zeitsch. f. Chemotherapie, 1912, vol. 1, No. 1, p. 44.

² Deutsch. Zeitsch. f. Nervenheilk., 1913, vol. xlvii and xlviii, p. 783.

³ Zeitsch. f. d. Ges. Neurol. u. Psychiat., 1913, vol. xvi, Nos. 1 and 2, p. 219.

⁴ Jour. Amer. Med. Assoc., 1913, vol. lxi, No. 1, p. 13.

⁵ Münch. med. Woch., 1913, No. 49, p. 2713.

3. Proteins in the presence of an electrolyte inhibit precipitation in colloidal gold solutions—the so-called “Gold-Schutz.”

The relation existing between this opposed reaction of electrolyte and protein is definite for the same protein, but differed when a different protein is used, and is therefore a specific property of the individual protein.

Lange first applied these principles to the investigation of sera, but the results were without significance. In spinal fluids, however, he found differences between normal and pathological specimens, when he varied the Zsigmondy technique by decreasing the concentration of the NaCl solution to 0.4 per cent., a concentration which in itself would have no effect upon the colloidal gold, but sufficiently strong to prevent the precipitation of globulin and nucleoproteins, both of which substances often occur in pathological spinal fluids.. This latter technique was also used in the study of sera, but no consistent changes were observed in pathological or normal sera.

Briefly the Lange theory is (1) That substances in pathological spinal fluids will precipitate colloidal gold provided the globulin and nucleoprotein fractions are held in solution with a 0.4 per cent. sodium chloride solution, and (2) that there is a characteristic change for certain diseases involving the central nervous system.

The technique is comparatively simple and requires the following materials:

1. Double distilled water, free from protein substances and rubber extractives.

2. One per cent. solution of gold chloride (Merck) in double distilled water.

3. Two per cent. solution of potassium carbonate (Baker & Adams Chemical Company) in double distilled water.

4. One per cent. solution of formalin (commercial) in double distilled water.

5. Ten per cent. solution of sodium chloride in double distilled water.

6. Jena beakers of 1500 c.c. to 2000 c.c. capacity (preferably the tall form).

7. One 1 c.c. pipette. graduated in hundredths and four or five 10 c.c. pipettes.

At first we encountered considerable difficulty in preparing the “reagent.” In spite of every precaution to duplicate the technique poor reagents occasionally resulted. Various factors which might influence the change to the colloidal state were separately studied. We found very rapid heating was apparently an important essential. We believe that the preparation of a good, translucent, “high red” reagent with a slight blue nuance which does not precipitate on standing is largely dependent upon freeing the distilled water from the gases in solution.

Our method is to heat 500 c.c. of doubly distilled water in a Jena beaker to 60° C., add 5 c.c. of the gold chloride solution, and follow with 5 c.c. of the 2 per cent. potassium carbonate solution. As the heating continues two types of bubbles are noticed: (1) those which come from the bottom of the beaker and are moderately large, and (2) those which arise generally throughout the liquid and are at first very small and gradually increase in size, and finally disappear after one or two minutes of boiling. As soon as these latter bubbles cease to arise the flame is withdrawn and 5 c.c. of the formalin solution are added. The beaker is given a rotary motion to aid in the rapid diffusion of the formalin. It is our experience that unless the color change is almost instantaneous the resulting reagent will be poor. By following this technique we have been able to secure reagents that are macroscopically identical. This reagent can be made up in considerable quantity, and apparently lasts indefinitely.

The technique of setting up the test is as follows: A suitable amount of 10 per cent. salt solution is diluted with double distilled water, so that the resulting strength is 0.4 per cent. For a single test a row of ten test-tubes, chemically clean, are placed in a rack and 1.8 c.c. of the 0.4 per cent. salt solution are added to the first tube and 1 c.c. to each of the succeeding tubes; 0.2 c.c. of spinal fluid, free from bacterial contamination, hemoglobin admixture, or red-blood corpuscles is added from a 1 c.c. pipette to the first tube. Thorough mixing is secured by pipetting in and out two or three times, and 1 c.c. is removed from this tube to the second, which is mixed in the same way. One c.c. is removed from the second tube and placed in the third tube, and so on until the ten tubes are treated in the above manner; the last tube will have 2 c.c. in it; 1 c.c. is withdrawn and rejected. In this way the dilutions are increased by geometrical progression, in the order 1 to 10, 1 to 20, 1 to 40, and so on up to 1 to 5160. After the specimens to be tested have been treated in the above manner, 5 c.c. of the reagent are added to each tube, which is shaken immediately after the addition. Although the change is very pronounced in many instances within a few minutes after the addition of the reagent, the readings are much more distinct when taken twelve to twenty-four hours after the test is set up.

In pathological fluids the change in color of the reagent is gradual in the series. A single tube showing marked change is always to be regarded with suspicion. Such tests are always repeated, and the usual result is uniformly graded reactions. Specimens from cases which have been receiving salvarsanized serum intradurally are excepted. Tests showing a change in only one tube upon repetition are usually found to be negative.

The success of the test depends upon (1) the use of scrupulously clean glassware; (2) accuracy in all measurements (for this reason

the same 1 c.c. pipette is used for every spinal fluid), (3) bacterial contamination in spinal fluids should be avoided.

We studied the effect of the introduction of bacteria into fluids giving a positive reaction. Bacterial contamination weakens the reaction and a considerable contamination may change a positive reaction to a negative. Spinal fluids kept "bacteria-free" have given the same reaction for weeks.

In Table I a group of typical reactions is indicated by expressing the color change with numbers, \pm representing the slightest increase

TABLE I.—TYPICAL REACTIONS.

Dilutions of cerebrospinal fluid	10	20	40	80	160	320	640	1280	2560	5120
Syphilis, weak		2	3	4	4	3	1	0	0	0
Syphilis, strong	1	4	5	5	5	5	5	5	3	0
Tubercular meningitis	\pm	\pm	\pm	\pm	2	4	2	0	0	0
Purulent meningitis	\pm	\pm	\pm	1	2	3	4	5	3	1
Negative	0	\pm	\pm	\pm	0	0	0	0	0	0

in blue tint, 1 a slightly greater change, and so on through 5, which represents an absolutely colorless solution. The maximum intensity of change and not the quantitative amount of change has diagnostic value. All readings were made in one hour and confirmed the next day.

In Table II the cases are grouped together with routine laboratory examinations of blood and spinal fluids and clinical diagnoses. We have taken 100 consecutive cases with 122 tests and have compared the results obtained by the gold reaction with the clinical diagnoses and other "laboratory tests."

In Group I, clinically diagnosed as Tabes, the gold reaction agreed with the clinical diagnosis in every case. In 9 of these cases the blood and spinal fluid were negative to the Wassermann reaction. In two cases all other laboratory data listed were negative; the patients had an acknowledged syphilitic history and the clinical evidences of tabes. In a second case the other data were negative except for the increased cell count.

In Group II, clinically general paresis, a positive gold reaction for syphilis was obtained in all cases with one exception, which was an early general paresis. In this case the other laboratory findings listed were also negative, clinical examination being the sole basis for diagnosis. The Wassermann reaction was particularly effective in this group.

Group III, cerebrospinal syphilis, is not noteworthy except in the relative intensity of the resulting gold reaction. Half of these cases show a strong reaction, being in this respect comparable with those of general paresis and greatly exceeding those of tabes, which only showed 25 per cent. of strong reactions.

TABLE II.

Disease.	Cases.	Tests.	Blood.				Spinal fluid.				Gold reaction.								
			Wassermann.		Wassermann.		Cells.		Globulin.		Typical reaction for syphilis.	Positive reaction not typical of syphilis.	No reaction.						
			+	—	+	—	5 or more.	Less than 5.	+	—									
Tabs	24	28	4	12	2	6	11	12	1	..	10	11	3	7	10	..	28	..	1
General paresis	12	17	8	3	1	..	10	1	1	..	10	1	1	9	1	1	16	..	
Cerebrospinal syphilis	8	10	3	3	2	..	6	..	2	..	8	7	..	1	10	..	
Cerebral syphilis	3	3	1	2	3	1	1	1	1	..	2	3	..	1
Spinal syphilis	4	5	3	..	1	..	3	1	3	..	1	3	..	1	4	..	1
Mental diseases	8	8	2	6	1	7	4	4	..	3	5	3	..	5
Tuberculous meningitis	4	5	1	1	2	1	3	4	4	5	
Purulent meningitis	1	4	1	1	1	1	4	
Epidemic cerebrospinal meningitis	1	2	1	1	1	1	2	
Influenzal meningitis	1	1	1	1	1	1	1	
Brain tumor	2	2	..	2	2	2	1	..	1	..	1	1
Poliomyelitis	1	2	..	1	1	1	1	2
Epilepsy	1	1	1	1	1	1	1
Miscellaneous diseases	15	15	..	15	1	2	10	3	1	7	7	15
Syphilis, but not of the central nervous system	8	9	4	1	3	8	2	5	1	..	4	4	4	..	5
Cases giving conflicting reaction	7	10	..	5	2	7	7	1	3	3	7	..	3

+ = positive. — = Negative. ± = Doubtful. ○ = Data not obtained.

Group IV, cerebral lues, presents one interesting case which was clinically diagnosed as polioencephalitis, and which later showed a typical gold reaction for syphilis. A syphilitic etiology was confirmed by a positive blood in spite of a negative spinal fluid to the Wassermann reaction. The patient died two weeks after the test, but there was no autopsy. A second case was negative to the Wassermann reaction in spinal fluid and blood, and the cell count was not increased, and there was no record of the globulin content. The gold test was positive.

Group V, spinal syphilis, contains a case of gumma of the cord in which all laboratory data except increased globulin content were negative. The gold reaction was also negative. This case improved under salvarsan. A second case was negative to the gold upon first examination, but later showed a positive result on another spinal fluid, the case being clinically syphilis, with a previous positive Wassermann reaction.

Group VI, which includes dementia precox, manic-depressive insanity, delirium tremens, alcoholic delusions, and a moral defective, shows the following analysis: One case of manic-depressive insanity with a positive Wassermann reaction on the blood had a gold test positive for syphilis. This latter result is not, however, absolutely trustworthy because of a slight blood tinge in the specimen of spinal fluid examined. Another case with a positive Wassermann blood and spinal fluid in a moral defective gave a positive gold test. A third case of questionable dementia precox in a woman, aged thirty-seven years, in which all the evidence was negative except that the spinal fluid was obtained under increased pressure, gave a positive reaction to the gold test. We have noted a number of cases clinically dementia precox which gave a positive Wassermann reaction in blood and spinal fluid or both.

Groups VII, VIII, IX, and X include the cases of meningitis. In the gold test all gave the changes of color in the high dilutions of the gold solution. (See Table I.) These reactions are easily differentiated from the reactions in the lower dilutions that are typical of syphilis.

Group XI. Two cases clinically brain tumor, one negative to the gold, but not typical of syphilis. The positive reaction in this case is similar to the reaction of tubercular meningitis.

Group XII. The one case of poliomyelitis on which two tests were done, gave negative gold reactions.

Group XIII. A case of epilepsy with other negative findings except a moderately positive Wassermann reaction on the blood, gave a negative gold reaction.

Group XIV consists of acute and chronic disease in which syphilis could be excluded with clinical certainty and gave a negative gold reaction in each case. This group includes one case of cerebral hemorrhage.

Group XV includes cases of syphilis, but with no evidence of any lesion in the central nervous system. The gold test was positive in four tests on three cases, all of which had positive Wassermann reactions in the blood.

The last group is summarized briefly as follows:

A case of cancer of the intestine which gave a positive and a negative gold reaction on the same fluid. The tests, however, were at intervals of over a week and the resulting bacterial contamination would easily account for this difference.

A case of gastric ulcer, with the same type of reaction as above, in which autopsy revealed gastric ulcer. The history was suspicious of syphilis, and the autopsy being a restricted one, gave no opportunity for examination of the spinal cord.

A case of acute pancreatitis, tested in our earlier experience with the reaction, gave a somewhat doubtful change.

A case of arteriosclerosis, with other negative findings for syphilis, gave a positive gold for this disease.

A case of pernicious anemia with nerve symptoms, which had been given salvarsan, showed a positive gold reaction for syphilis.

A doubtful case in a boy, aged four years, in whom either tubercular meningitis, poliomyelitis, or acute gastro-enteritis with cerebral symptoms was suspected, gave a positive reaction for syphilis on repetition.

A case with cancer of the stomach gave a positive and negative reaction under the same conditions as the second case. Autopsy revealed cancer of the stomach. The central nervous system was not examined.

In our experience the cases with syphilitic etiology do not give reactions typical for the resulting disease. For instance, it is not possible to differentiate between tabes, general paresis, and cerebrospinal syphilis, etc., except as above noted, that the reaction is more likely to be strong in general paresis and cerebrospinal syphilis.

Just how the reaction takes place and to what protein it is due is not known, and our study throws no light upon the question.

DISCUSSION AND SUMMARY.—Scrutiny of the tables shows that the gold reaction is not parallel with the blood Wassermann reaction, the spinal fluid Wassermann reaction, the globulin or the cell count, but apparently more constant in syphilitic affections than any of the other tests.

The blood Wassermann reaction is present in only 43 per cent. of the cases diagnosed as syphilis of the central nervous system.

The Wassermann reaction on the cerebrospinal fluid was positive in 59 per cent. of the cases. Both were absent in 24 per cent. of the cases of presumable syphilis of the central nervous system. It is obvious then that it is not possible to exclude syphilis of the central nervous system on the basis of the Wassermann reaction on the blood or cerebrospinal fluid, or both.

Cell counts above 10 were found in 63 per cent. of the cases of syphilis of the central nervous system, and the counts were below 10 in 27 per cent. of the cases diagnosed as syphilis of the central nervous system. Cell counts under 5 are certainly within normal limits. Counts of 5 to 10 are doubtful. Counts above 5 were present in 75 per cent. of the cases. However, the cell counts are found in other conditions than syphilis beside purulent meningitis, notably tubercular and influenzal meningitis, anterior poliomyelitis, and brain tumor. One of us (Lee) has observed a cell count of 53 shortly after a uremic convulsion, in which case two days later the count was 0. The other tests were negative. The colloidal gold test was not done in this case. The cell counts are of distinct value, as an abnormal count is found in a high percentage of cases of syphilitic affection of the central nervous system. The value of cell counts is somewhat impaired by the fact that other conditions which may be confused clinically with syphilis often show a great increase in the number of cells.

The globulin test (Noguchi's⁶ butyric acid test and Nonne's⁷ ammonium sulphate test) has not been satisfactory in our hands. A standard of positive and negative reactions is difficult and ill-defined. There were many doubtful reactions.

The globulin test was positive in 77 per cent. of tested cases of syphilis of the central nervous system. This test is also positive in cases of tubercular meningitis, brain tumor, and other conditions.

The gold reaction typical of syphilis has occurred only twice in the absence of blood Wassermann reaction, spinal fluid Wassermann reaction, cell counts, and globulin. In both these cases the gold reactions were confirmed by the clinical diagnosis. The gold reaction usually occurs in combination with one of the other tests, but there is no constant association with any test. A gold reaction typical for syphilis has been obtained in the absence of each of the other tests. A negative gold reaction was obtained in only two cases in which the condition of the central nervous system was diagnosed as syphilitic.

The diagnosis of these cases is often difficult, and is occasionally determined by the laboratory findings. We have accepted the clinical diagnosis as final.

The disadvantages of the test are that the presence of blood or serum vitiates the findings, and that a certain amount of care must be used to prevent extraneous protein substances from contaminating the fluid or the reagent.

The advantages of the test are the small amount of cerebrospinal fluid required, 0.2 c.c., its technical simplicity, the sharpness of the reaction, and its delicacy.

⁶ Serum Diagnosis of Syphilis (2d edition), p. 155.

⁷ Syphilis and the Nervous System (translated by G. Ball), p. 341.

CONCLUSIONS. A gold reaction typical for syphilis is nearly constant in cases of syphilis of the central nervous system.

This test is more delicate than the blood Wassermann reaction, spinal fluid Wassermann reaction, cell count, and globulin content.

The test has the advantage that it gives a reaction with pathological spinal fluids due to other causes than syphilis, that is characteristic and easily differentiated from the reaction typical for syphilis.

Our experience confirms the findings of other observers that the gold test is delicate, and that the margin of error is exceedingly small.

THE EFFECT OF EXTRACTS OF SHEEPS' THYROID AND OF PATHOLOGICAL HUMAN THYROID UPON THE FATIGUE CURVE OF VOLUNTARY MUSCLE

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MUSCULAR weakness, independent of the emaciation which develops sooner or later as a feature of Graves' disease, is a symptom which has impressed many observers of this condition. Dock¹ in his article upon exophthalmic goitre in Osler and McCrae's *Modern Medicine* discusses this feature as follows: "Muscular weakness is another characteristic symptom. It is so rarely absent that it is strange that Askanazy's finding of muscular atrophy and degeneration has not been more widely confirmed. Fr. Müller gives some characteristic measurements showing the degree of weakness."

	Basedow's disease.		Normal woman.	
	Kilograms.		Kilograms.	
	R.	L.	R.	L.
Shoulder, adduction	3.8	3.6	13	12
Shoulder, abduction	1.9	1.5	15	12
Elbow, flexion	4.8	4.0	30	25
Elbow, extension	5.6	4.8	18	14
Finger, flexion	6.5	5.5	20	18
Hip-joint flexion	4.6	4.1	30	
Hip-joint extension	5.1	4.6	35	
Hip-joint adduction	4.5	4.5	15	
Hip-joint abduction	4.0	4.0	15	
Knee flexion	7.1	6.6	30	
Knee extension	13.4	12.1	40	

As a further development of the same line of observation, a definite muscular syndrome, that of myasthenia gravis, is not

¹ Exophthalmic Goitre, Osler and McCrae, 1909, vol. vi.

infrequently associated with exophthalmic goitre. Since 1877, when Wilkes reported the first case of myasthenia gravis, we find 197 recorded cases. In these reports there are 8 cases of pronounced combination of the two conditions.² If this were all we should still be within the realm of coincidence, but the facts that comparatively few nervous diseases, with the exception of hysteria, chorea, and paralysis agitans, complicate exophthalmic goitre and that many clinicians (Oppenheim, Kalischer, Goldflam, Finizio, Karplus, Murri, Warner, Bristowe, Ballet, Finlayson, Liebrecht, Rothmann, Marina, Camuset, Suckling and others) have observed some of the symptoms of Graves' disease in profound cases of myasthenia gravis, and *vice versa*, lead us rather forcibly to the idea of a closer connection. We can, therefore, as Goldflam expresses it, "accept a certain relation between the two diseases, because the combination of asthenic palsy with prominent or mild symptoms of Basedow's disease occurs so often, rather than speak of a mere coincidence of occurrence. This is also the opinion of Oppenheim."³

Experiments with thyroid feeding have been most unsatisfactory in regard to producing a definite picture of exophthalmic goitre, but weakness—not certainly dependent upon loss of weight—has appeared. Unfortunately, this symptom has not been specially considered in endeavors to produce hyperthyroidism in animals, which too often have been taken up with attempts to estimate less measurable and controllable criteria, such as nervousness, exophthalmos, tachycardia, etc. Opinions are united upon the harm done by administering thyroid in pronounced cases of Graves' disease, and we find no well-watched cases of myasthenia in which thyroid has been helpful, whereas there are several in which it has seemed to augment the condition—a fact necessitating prompt withdrawal. Added to this, Rennie⁴ reports a rapidly fatal case of myasthenia gravis in a jockey who had been taking large quantities of thyroid to reduce his weight, but who presented no evidence of exophthalmic goitre.

Mosse⁵ administered thyroid material to two hospital patients who had been taught to use the ergograph, and believed he secured evidence leading to the conclusion that their muscular power was increased. His experiments are few and his results not beyond the possibilities of error with this apparatus. Markeloff⁶ injected glycerin extracts of thyroid into dogs and found a slight degree of resistance to fatigue. He believes thyroid markedly increases the irritability of the neuromuscular apparatus. His dosage of

² Arch. f. Psychiat., 1886, xvii, Hefte 2 (Jendrassik); Berlin. klin. Woch., 1899, xxxvi, p. 574 (Reinak); Arch. de Neurol., 1905, xix (Brissaud and Bauer); Zeitsch. f. Augenheilk., 1904, xii (Loeser, 2 cases); Neurolog. Centralbl., 1904, vol. xxiii (Meyerstein); Rev. Neurol. and Psych., 1908, vi (Rennie); *ibid.*, 1913, vol. xi (Rennie).

³ Goldflam, Neurolog. Centralbl., 1902, vol. xxi, p. 305.

⁴ Australasian Med. Gaz., May, 1904.

⁵ Arch. de Physiol., 1898, vol. x.

⁶ Oboz. Psik. Neurol., etc., St. Petersburg, 1912, vol. xvii.

thyroid in view of Carlson's⁷ observations upon the resistance of dogs to thyroid material would seem to be extremely small, and if a positive effect can be obtained by such light administration it is most remarkable. Ioteyko⁸ made Ringer's solution extracts of Merck's dried sheep thyroid, which correspond in strength to the 2 per cent. solutions used by ourselves. Immersion of frogs' muscles in such solutions gave evidence of stimulation. Similar experiments using Armour's thyroid gave no results in our hands.

EXPERIMENTAL WORK.—In view of such incomplete testimony as to the action of commercial thyroid material upon muscle, it became necessary to make some experiments with it before attempting to use material recognized as being abnormal. For this purpose the desiccated sheeps' thyroid prepared by Armour & Co. was selected. It is said to contain 0.2 per cent. of iodine. A weighed quantity of this powder was macerated in Ringer's solution isotonic for the frog.⁹ This maceration was carried on in the ice-chest over-night, and in the morning the filtrate contained the substance used in the experiments. By such a method only a small amount of the original material is represented in the filtrate, as the dried gland is but slightly soluble. For purposes of convenience, however, we term filtrations which resulted from the use of 5 grams of dried thyroid per 100 c.c. of Ringer's solution, 5 per cent. solutions; those which before filtration contained 1 gram, 1 per cent. solutions, and so on throughout the entire series. A 3 per cent. solution is straw-colored, clear, slightly viscid, and faintly acid to litmus. Experiments have been made at room temperature and at all seasons. Frogs have been the test animals. Different varieties gave identical results. Direct stimulation has been used throughout.

TECHNIQUE.—A cannula was inserted into the right branch of the truncus arteriosus, the left being tied and the sinus venosus opened. When the perfusion was ready to start, one leg was amputated at the thigh and the stump tightly ligatured. The perfusing fluid was turned on and allowed to run for ten minutes. By this method the head is not perfused but the abdominal vessels remain in the circuit; 4 to 5 cm. a minute was the rate employed, maintained evenly by a burette constructed upon the Mariotte principle.

Both legs are thus deprived of the normal circulation at the same time. The leg first amputated lies for ten minutes bathed in its own lymph, the other is perfused with the test solution. The two gastrocnemii are placed in separate muscle chambers, but in the same electrical circuit and record simultaneously. Maximal single break shocks at the rate of thirty-four per minute have been used, Edison and Laland cells being the source of the current.

⁷ Amer. Jour. Phys., 1912, vol. xxx.

⁸ Jour. Med. de Bruxelles, 1903, Nos. 27 and 29.

⁹ Sodium chloride, 0.7 per cent.; potassium chloride, 0.03 per cent.; calcium chloride, 0.026 per cent.

With such preparations one may make the ordinary fatigue curves upon a slowly moving drum or superimposed curves, in this last case recording every seventy-fifth contraction.

By this technique a number of tracings were made, using Ringer's solution alone. There was no evidence of depression. The muscles made identical curves or else the perfused one performed a small amount more work.

Tracing 1 shows the effect of 3 per cent. thyroid. There is slight stimulation followed by early and marked depression. Tracing 2, the superimposed curve with the same solution, shows an identical result. Tracings 3 and 4 illustrate the effects of a 1 per cent. solution, which is indistinguishable from that of pure Ringer's solution. We found no result below 1 per cent., at which point there was evidence of stimulation occasionally. At no strength of solution was there evidence of distinctive effect, as, for instance, that of veratrin. The thyroid produced nothing except a simple quantitative lack of efficiency.

COMPARATIVE EXPERIMENTS WITH PATHOLOGICAL HUMAN GLANDS.—The glands used in the following experiments were taken from the operating-room in a sterile jar and minced aseptically. They were then dried in a current of air filtered through four layers of surgical gauze at a temperature from 40° to 50° C. Complete drying took a variable amount of time, but there was no odor nor evidence of gross contamination. After drying, the glands were finely powdered and then extracted with light gasoline¹⁰ in Soxhlet extractors to render them fat-free. This process parallels that used by Armour & Co. in the preparation of sheeps' thyroid, with the exception that the sheeps' glands are collected without aseptic precautions from animals which have been thoroughly bled. After fat extraction the dried powder was placed in sterile bottles and left until used; the technique of making solutions and records was the same as we have detailed for sheeps' thyroid. As the individual glands yield small amounts of dried material, 3 per cent. solutions have been the strongest employed.

PATHOLOGICAL GLAND IV.—The patient, Mrs. R., aged twenty-one years, one year before operation noticed that her neck was swollen and immediately began to complain of tremor, tachycardia, great nervousness, and exophthalmos. These symptoms continued until April 22, 1912, when she was operated upon by Dr. G. P. Müller. Following the operation there was an explosion of hyperthyroidism, but later she progressed favorably. The case was diagnosed clinically as one of pronounced Graves' disease. Grossly the gland contained a few colloid cysts but was largely pale, meaty thyroid tissue. The microscope showed a characteristic cellularity and increase in mucoid material.

¹⁰ Gasoline, SS°, Baumé, fractional distillation yields 65 per cent. below 60° C., and practically 100 per cent. below 100° C.

Tracing 5 shows the effect of a 3 per cent. solution of this gland. There is a large amount of depression accompanied by irregularity.



FIG. 1.—Upper muscle normal. Lower muscle 3 per cent. sheep's thyroid. Thirty-four stimuli per minute.

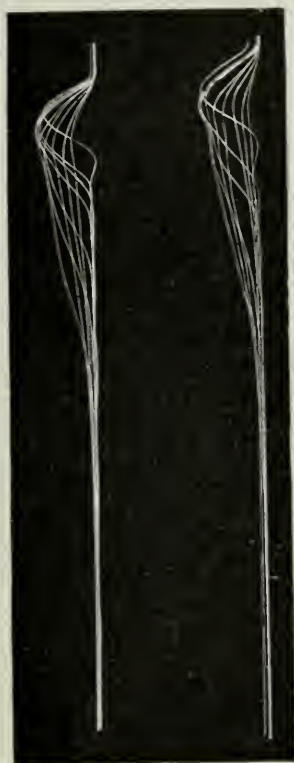


FIG. 2.—Superimposed curve. Upper muscle normal. Lower muscle 3 per cent. sheep's thyroid. Thirty-four stimuli per minute. Seventy-fifths recorded.

This irregularity was observed occasionally in our tracings made with sheep's thyroid, but was rare. In those made with glands

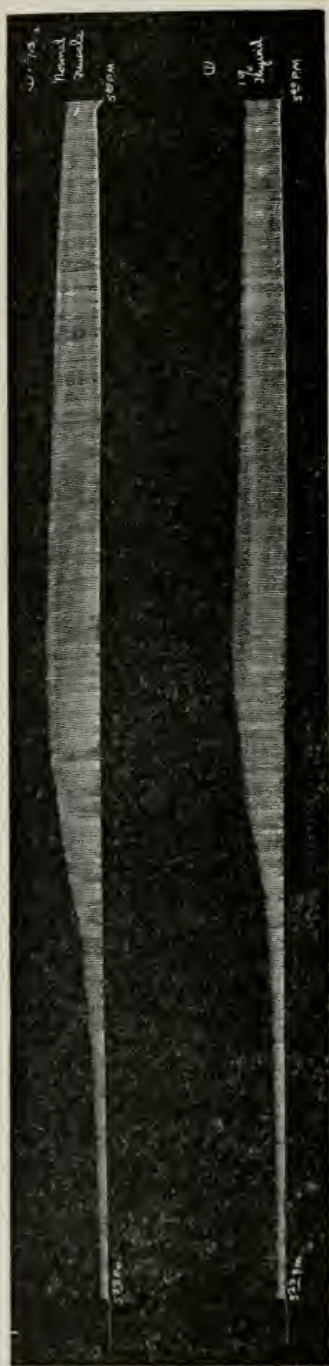


Fig. 3.—Upper muscle normal. Lower muscle 1 per cent. sheeps' thyroid. Thirty four stimuli per minute

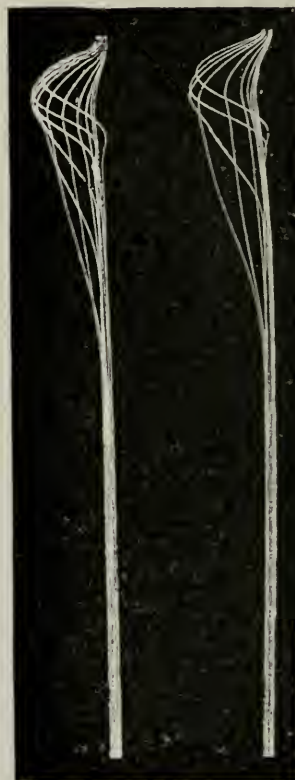


Fig 4 —Superimposed curve. Upper muscle normal. Lower muscle 1 per cent. sheeps' thyroid. Thirty-four stimuli per minute. Seventy-fifths recorded.

from cases of Graves' disease it occurred constantly. Tracing 6 demonstrates an identical result. Tracings 7 and 8 show the effects of a 1 per cent. solution. There is slight stimulation, as we sometimes found to be the case with similar strengths of sheep's thyroid.

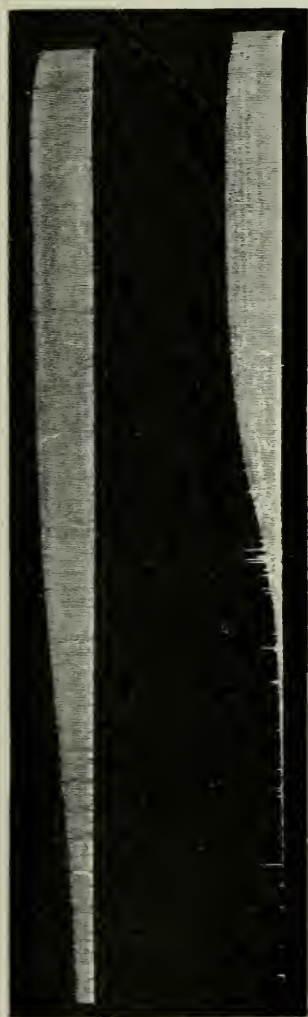


FIG. 5.—Upper muscle normal. Lower muscle 3 per cent. gland IV (pronounced Graves' disease). Thirty-four stimuli per minute.



FIG. 6.—Superimposed curve. Upper muscle normal. Lower muscle 3 per cent. gland IV (pronounced Graves' disease). Thirty-four stimuli per minute. Seventy-fifths recorded.

PATHOLOGICAL GLAND V.—The patient, Mrs. S., aged fifty-four years, had suffered from a disfiguring goitre for many years, which had been increasing rapidly in size during the two years prior to operation. At the time of operation she was able to swallow liquids alone, and had become exceedingly emaciated. There

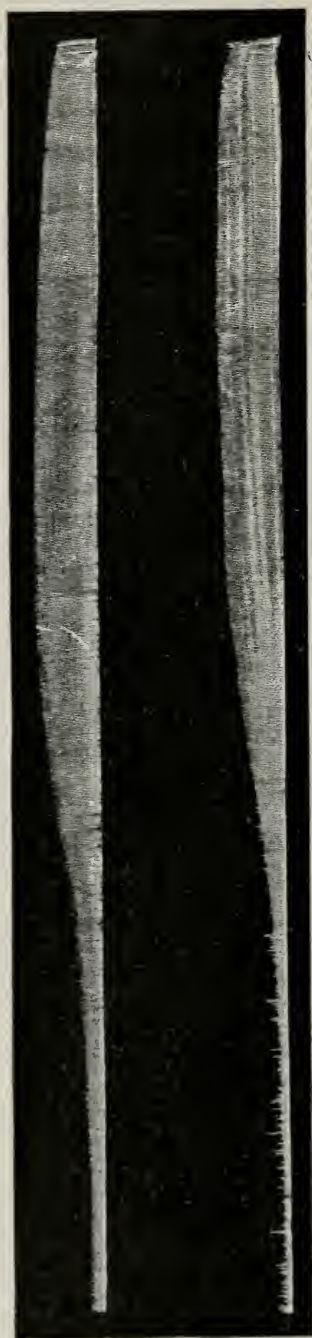


FIG. 7.—Upper muscle normal. Lower muscle 1 per cent. gland IV (pronounced Graves' disease). Thirty-four stimuli per minute.



FIG. 8.—Superimposed curve. Upper muscle normal. Lower muscle 1 per cent. gland IV (pronounced Graves' disease). Thirty-four stimuli per minute. Seventy-fifths recorded.

were no symptoms of Graves' disease or myxedema. Dr. C. H. Frazier removed the gland, which was diagnosed pathologically as

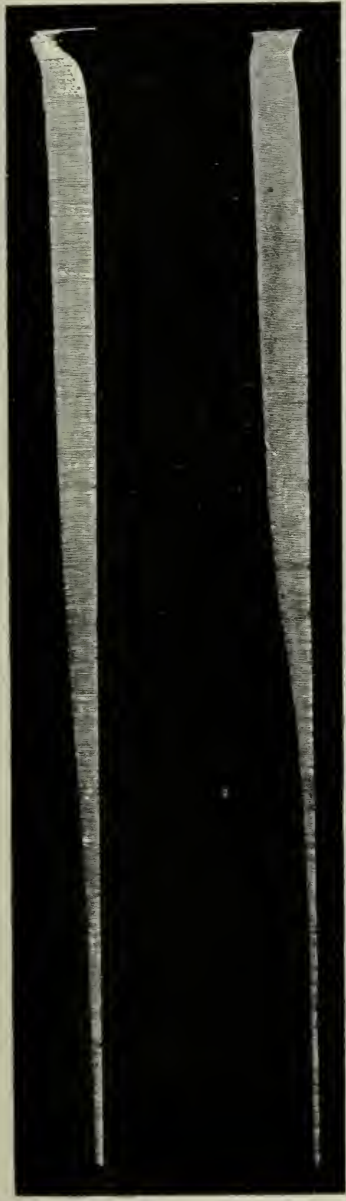


FIG. 9.—Upper muscle normal. Lower muscle 3 per cent. gland V (colloid goitre). Thirty-four stimuli per minute.

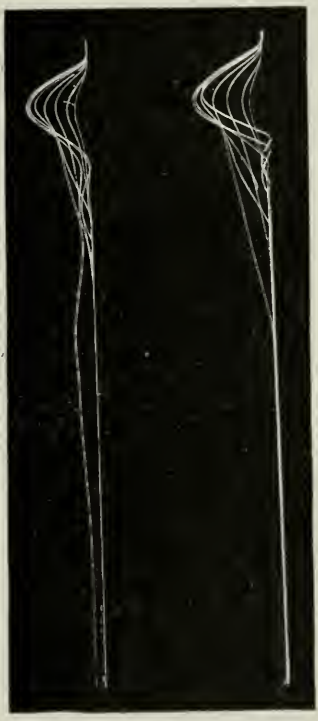


FIG. 10.—Superimposed curve. Upper muscle normal. Lower muscle 3 per cent. gland V. Thirty-four stimuli per minute. Seventy-fifths recorded.

a colloid adenoma. It was made up entirely of large and small cysts filled with colloid material.

Tracings 9 and 10 illustrate the effect of 3 per cent. solutions. The thyroid muscle has done as much work as the normal, and the absence of irregularity is easily seen; 1 per cent. solutions were without effect.

In all we have experimented with material removed from nine thyroid cases. Of these three were pronounced colloid goitres operated upon for pressure symptoms and for disfigurement. Perfusion with 3 per cent. solutions of these glands gave no result in two cases and a slight suggestion of depression in one; 1 per cent. solutions were without effect. The tracings never showed the irregularities we have mentioned in connection with the parenchymatous goitres. Two cases were indefinite types clinically and pathologically. They occurred in girls of sixteen and seventeen, nervousness and slight enlargement of the thyroid being the chief symptoms. With one we obtained no result by 3 per cent. perfusion. In the other, which was as nearly normal human thyroid as one could obtain, we obtained depression, but of a less pronounced type than with our sheeps' thyroid or with our parenchymatous goitres. In the four remaining cases there was undoubted Graves' disease, the severity of which varied. In one there had been a tumor of the thyroid for a year. Exophthalmos and palpitation were beginning, but the patient could still work, and asked for operation mainly on account of disfigurement. Her gland after removal showed active hyperplasia, absence of colloid, and large amounts of mucinous material; 3 per cent. extracts caused marked depression, but none of the irregularity characteristic of our other cases. The other three cases were pronounced types of Graves' disease. Tracings from these glands made a most uniform picture following the type illustrating this paper. Depression and irregularity were the features.

Since the cystic colloid glands contain a large amount of material insoluble in water, it is reasonable to assume that their solutions contain a lower percentage of extractives than those of pure parenchymatous goitres. Disregarding the question as to whether or no solutions of dried gland contain the unknown active constituent of the thyroid, it is possible that our uniform effects may be due to a difference in strength of solution which the difference in solubility indicates. This matter could be controlled if we had access to large numbers of glands and could use those from which pure colloid could be obtained. It must be noted, also, that the experiments with both types of pathological glands were done during March and April. This may account for the irregular contractions we have observed in our parenchymatous gland cases. Controls with pure Ringer's solution and colloid gland solutions failed, however, to give irregularities during the same period.

CONCLUSIONS.—1. Ringer's solution extracts of dried sheeps' thyroid caused depression in 3 per cent. solutions made after our

technique. The depression gave way to slight stimulation between 1 and 2 per cent. of strength. At 1 per cent. there was usually no effect distinguishable from pure Ringers' solution.

2. Similar material from cases of Graves' disease gave an equal amount of depression. Clinical observation upon myasthenia gravis and exophthalmic goitre is suggestive in this relation. In addition there was irregularity in the strength of contractions, but the series is much too small to call this a specific attribute.

3. Extracts from cases of colloid goitre gave in most cases no depression; and in all less depression than was obtained with either the sheeps' thyroid or with extracts of parenchymatous goitres. There is no irregularity in the strength of contractions such as was noticed with the latter type.

FURTHER EXPERIENCES OF THE TREATMENT OF IMPERFECTLY DESCENDED TESTICLES.

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SOME months ago I was asked by a doctor "how I treated cases of imperfectly descended testicles now," and appreciated clearly how impossible it was to give an answer sufficiently concise to be clear enough to satisfy the hearer. Going home, I communed with the records of the cases which I had done in the last ten years, *i. e.*, since I published a full account of my opinions and practice on the subject. In the number of the *British Medical Journal* for June 4, 1904, I published a paper on "The Value of the Imperfectly Descended Testicle, the Advisability and Value of the Operations Performed for its Relief." Since then a period of about ten years has elapsed, bringing much experience, which must of necessity have modified the conclusions arrived at in 1904. The advance of time has increased my interest in the subject, while the further experience has added to knowledge of the pathology of the condition and the results of treatment.

To begin, the imperfect descent of the testicle is in almost all cases a congenital malformation or deformity, due to some condition (or conditions) which, by depriving the gland of its full power of development, has arrested it in the course of its descent. The congenital malformation under consideration is practically always associated with arrested development of the tunica vaginalis, leaving, at least, a potential hernia sac. In the associated deformity the tunica vaginalis remains in communication with the peritoneal

cavity, a condition disposing to the development of a hernia, a total hernia sac.

Upon being confronted with a patient with imperfect descent of the testicle, it is often impossible to decide if the condition of imperfect descent is temporary or permanent; that is to say, is the testicle merely belated in its descent or not? Various people arrive at the same stage of development at various times. So long as no hernia is present, there need be no hurry in determining the answer to this question. Neither need there be any hurry if the malformation is only unilateral.

This expectant attitude is terminated either by:

1. The recognition of a hernia accompanying the imperfect descent, or

2. The recognition that the imperfect descent is not mere belatedness.

Either of these two occurrences terminates the period of waiting and indicates the need for active treatment, operation. As these factors are only two in number, it is well to consider how and why they indicate the termination of the period of inactivity and initiate that of activity.

HERNIA. The presence of hernia in association with an imperfectly descended testicle indicates the fact that operation is necessary for its cure. Indeed, there is no other treatment for the hernia; a truss would press on the testicle or its vessels. Moreover, *the non-separation of the tunica vaginalis and peritoneum prevent the testicle from descending*, even if it were capable of doing so. The hernial sac holds the gland up. Hence the cure of the accompanying hernial sac, by nature or art, will aid the testicular anomaly to be cured. In separating the sac from the cord, great care must be exercised to avoid injury to the vessels, for such an injury is known to militate greatly against the testicle subsequently having any physiological value.

THE PERSISTENCE OF THE DEFORMITY. When the testicle has been imperfectly descended for sufficient time, say until the patient is seven years old, to show that the condition is a permanency and no temporary anomaly of a gland belated in its descent, it is necessary to operate. Such a proceeding may, in the main, be done in one of three ways:

1. The accompanying hernial sac may be divided and stripped of the cord, allowing the testicle to descend into the scrotum. Any but the mildest scrotal fixation is merely a prelude to failure, anatomical or physiological. Such an operation is called an *orchidoplasty* or an *orchidopexy*.

2. The gland may be removed as advocated by many. This line of treatment is especially indicated when the imperfect descent is unilateral. It is satisfactory in its after-results. The operation is an *orchidectomy*.

3. Especially when the condition is bilateral, the gland may be returned to the abdomen, intraperitoneally. Any internal secretion which the gland may have is retained which will aid the patient to develop sexual characters, such as hair on face, male voice, male body, energy of mind and body. Such an operation is an orchidocelioplasty.

Which of the three alternatives will be performed must to a great extent be decided by the surgeon at the operation. The great principle we do know about in these cases is that should the testicle be unable to furnish an external secretion of its own power, no amount of surgical art can make it do so; while clinical experience has shown how prone surgical art, in some form of orchidopexy, is to be followed by atrophy or fibrosis, the gland losing any power it might have possessed of developing any secretion, external or internal, that before the operation it might have been capable of doing. Hence it may be laid down that orchidopexies, except in unusual instances, rob the patient of something. Sufficient years have gone by for many workers and many patients to have proved this. As yet, surgeons have no great or extended experience of orchidoplasty. But some, myself among them, can witness that it is sometimes followed by growth and descent of the gland; most often the descent is not as great as is normal, and occasionally I have seen atrophy. But I can say that the more experienced a surgeon is with these cases the less likely he is to do an orchidoplasty in an unsuitable case, obtaining a failure. Still, as surgeons can only work with the material supplied them, it is impossible to attain a perfect success always. Imperfect success may be the greatest success that the provided material allows. In such doubtful cases an orchidocelioplasty is best. The results of this last operation are difficult to estimate. Though it has been done for about fifteen years, there is nothing much to be said except:

1. It has been urged on theoretical grounds that the returned testicles are prone to become malignant. This is not so.

2. It has been urged that in the intra-abdominal position, such common diseases as gonorrheal orchitis endanger life. This is not so.

3. Apparently the intra-abdominal position abolishes any external secretion, but preserves and encourages the internal secretion; an important point, as it is in the internal secretion above that practically the whole value of the imperfectly descended testicle lies.

It is the operation more frequently done in these cases than any other. In my own work for the last ten years the percentage has been: Orchidopexy, about 10 per cent.; orchidocelioplasty, about 50 per cent.; orchidoplasty, 40 per cent.

The great infrequency of the performance of the operation of orchidopexy is the result of an extended experience of the results

of that operation not only done by myself but also when done by others. These may be shortly generalized. The immediate result of the operation is fair. Then the testicle begins to ascend, usually until the gland is in the neighborhood of the pubic spine. Some of these organs descend again, taking upward of eighteen months to do so. Such cases are the best results of the operation, and until a few years ago I thought that the last word of criticism had been said. But further experience taught that this was not so. Atrophy of the gland may come on any time within about two years of the operation. Even if a gland is well placed by operation it may atrophy. A badly situated gland may atrophy. And the conclusion was borne in upon me that *the operation of orchidopexy more frequently fails from atrophy of the gland than by not retaining that gland in a good position.*

The treatment suggested for the condition of imperfectly descended testicles can be summed up from the point of view of the age of the patient, as the condition is a congenital one.

At birth and up to the age of about five years of age watch the case to decide if the testicle is merely late in its descent or not. If a hernia is seen to be present, operate and conclude by doing an orchidoplasty.

From seven to twenty years of age, operate if a hernia is present or not. Do either an orchidoplasty, an orchidectomy, or an orchidocoelioplasty.

Above twenty years of age, do an orchidectomy.

There is another point which further experience has taught me. In my book on the *Male Diseases of General Practice*, Oxford Medical Publications, pp. 95 to 97, the subject of the "masked imperfect descent of the testicle" is considered, I believe, for the first time. Shortly the imperfect descent of the testicle is marked if the hernia which accompanies it pushes the testicle down into the scrotum. Such a condition of imperfect descent is not recognized or recognizable until the hernia sac is fully stripped up and removed, the radical cure done. The testicle then assumes the position of imperfect descent or something near it. Since the publication of that book, in 1910, I have met many examples of this condition, and am sure that it is a great deal more frequent than I formerly supposed. Such a conclusion supports in detail Mr. Hamilton Russell's theory that every hernia depends for its cause on a congenital fault. Such a congenital fault with the tunica vaginalis is likely to be accompanied by some fault in the descent of the testicle. To put the question shortly, whenever a hernia is produced through a congenital fault, it is likely that the hernial-fault is accompanied by another in the descent of the testicle. The accompanying testicular fault may be hidden by the hernia pushing the testicle scrotumward. Thus the testicular anomaly will not be recognized until the sac of the hernia has been divided

and removed. These cases I find suitable for a scrotal orchidopexy, the operation adhesion bearing a similar relation to the testicular descent as the stick to the correct growth of the scarlet runner. This is the recognition and treatment of the condition of marked imperfect descent of the testicle.

OBSERVATIONS ON THE WASSERMANN REACTION.¹

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It is a well-known fact that there are great variations in the technique of the Wassermann reaction as conducted by different workers at the present time. Owing to these differences in technique it is not an uncommon thing for a clinician to receive contradictory reports of the test done on the serum of the same patient by different workers.

We wish to call attention to several factors in the technique which we believe are important in securing results upon which the clinician can always rely as a basis for treatment.

TITRATION OF COMPLEMENT. Many of the negative results obtained in cases of undoubted syphilis are unquestionably due to the employment of overdoses of complement and hemolytic amboceptor. The majority of descriptions of the Wassermann technique provide for double or triple doses of these reagents. The only possible reason for such excessive doses is to make allowance for and overcome any non-specific complement fixation on the part of the patient's serum or the antigen. By the method in use by us, the amount of complement available for specific fixation is the same as that required for complete hemolysis of one dose of corpuscles in the presence of one dose of amboceptor. We therefore avoid the excess of complement or amboceptor commonly used by many workers, though at the same time we do not neglect to provide sufficient complement to overcome non-specific fixation by serum or antigen. It is well known that there is some difference in the degree of non-specific absorption of complement by different sera. Browning and McKenzie go so far as to estimate the non-

¹ Read before the Pathological Society of Philadelphia, January 22, 1914, and received for publication February, 1914.

specific anticomplementary power of each individual serum to be tested as well as that of the antigen, and allow excess of complement corresponding to the sum of these doses in each individual case in reading the reaction proper. While this laborious and time-consuming procedure is theoretically correct, yet for practical purposes it is unnecessary. The non-specific absorption of complement varies so little with different sera, that in routine clinical work these variations can be ignored, and an allowance of complement based on the estimation of non-specific complement fixation in one case usually suffices for all. For our hemolytic system, we prepare a rabbit amboceptor in the usual manner of such strength that 1 c.c. of a 1 in 2000 or 1 in 3000 dilution will hemolyze 1 c.c. of a 5 per cent. suspension of washed sheep's corpuscles in the presence of 0.1 c.c. of complement. Having obtained a serum of this strength, in the test itself 1 c.c. of the amboceptor is employed in a fixed dilution of 1 in 1000, with the amount of complement necessary to cause hemolysis of the corpuscles when combined with this dose of amboceptor. Thus we do not titrate the amboceptor each time the test is made, but we do make a preliminary titration of complement.

Table I illustrates a titration for determining the minimal hemolytic dose of complement.

TABLE I.—A Titration for Determining the Minimal Hemolytic Dose of Complement.

	Incubation one hour at 37° C.			
	Complement 1 in 10 dilution.	Amboceptor 1 in 1000 dilution.	Sheep's corpuscles 5 per cent. suspension.	Result.
I	0.2 c.c.	1 c.c.	1 c.c.	Partial hemolysis.
II	0.3 c.c.	1 c.c.	1 c.c.	Almost complete hemolysis
III	0.4 c.c.	1 c.c.	1 c.c.	Complete hemolysis.
IV	0.5 c.c.	1 c.c.	1 c.c.	Complete hemolysis.
V	0.6 c.c.	1 c.c.	1 c.c.	Complete hemolysis.

In this case the minimal hemolytic dose of complement would be 0.4 c.c. of the 1 in 10 dilution. This dose makes no allowance for non-specific fixation by antigen and the patient's serum, and would therefore be insufficient for complete hemolysis in a negative case in doing the test itself. Instead, however, of employing double this amount of complement for the test itself, in order to determine the minimal hemolytic dose plus the non-specific fixation dose of complement due to the presence of serum and antigen, we make a preliminary incubation of different amounts of complement with 0.1 c.c. of pooled inactivated non-syphilitic sera and the dose of antigen to be used in the test. After incubation for one hour, the 1 in 1000 amboceptor and sheep's corpuscles are added, the tubes again incubated for one hour, at the end of which time the amount of complement in the tube in which hemolysis is just complete is taken as the amount required for the test proper, representing as it does the minimal hemolytic dose plus the amount absorbed non-specifically

by serum and antigen. This amount of complement usually ranges from 0.1 to 0.2 c.c. higher than the hemolytic dose alone, which if not allowed for, might cause a negative reaction to be read weakly positive, as by this method close readings are made.

Table II represents a titration of complement as carried out routinely before performing the tests proper.

TABLE II.—A Titration of Complement as Carried Out Routinely before Performing the Tests Proper.

	Incubation one hour at 37° C.			Incubation 1½ hours at 37° C.		
	Patient's serum, normal.	Antigen.	Complement, 1 in 10 dil.	Amboceptor, 1 in 1000 dil.	Sheep's corpuscles, 5 % sus.	Result.
I	0.1 c.c.	0.2 c.c.	0.2 c.c.	1 c.c.	1 c.c.	No hemolysis.
II	0.1 c.c.	0.2 c.c.	0.3 c.c.	1 c.c.	1 c.c.	Partial hemolysis.
III	0.1 c.c.	0.2 c.c.	0.4 c.c.	1 c.c.	1 c.c.	Almost complete hemolysis.
IV	0.1 c.c.	0.2 c.c.	0.5 c.c.	1 c.c.	1 c.c.	Complete hemolysis.
V	0.1 c.c.	0.2 c.c.	0.6 c.c.	1 c.c.	1 c.c.	Complete hemolysis.
VI	0.1 c.c.	0.2 c.c.	0.7 c.c.	1 c.c.	1 c.c.	Complete hemolysis.

In the titration illustrated the amount of complement required along with serum and antigen is 0.5 c.c., which, therefore, is the dose to be used in the test proper. It will be noted by comparison with Table I that this amount is 0.1 c.c. greater than the hemolytic unit of the particular complement serum used.

In quantitative estimation of the strength of the Wassermann reaction, we determine the number of hemolytic units of complement absorbed by a given serum in combination with the syphilitic antigen. Some syphilitic sera are capable of absorbing more than one hemolytic unit of complement, *i. e.*, of still giving complete or partial inhibition of hemolysis when two, three, or even more hemolytic doses of complement are used in the test. When desirable, therefore, additional tubes can be prepared containing two, three, or more units of complement plus the amount always to be allowed for non-specific fixation by serum and antigen.

Table III illustrates the results in a positive case of syphilis employing tubes containing one, two, and three units of complement, the unit of complement being based on the titrations given in Tables I and II. From this result we would say that the case was strongly positive, of a degree of two units.

TABLE III.—The Results in a Positive Case of Syphilis, Employing Tubes Containing One, Two, and Three Units of Complement, Based on the Titrations Given Above.

	Incubation one hour at 37° C.			Incubation one-half hour at 37° C.		
	Serum.	Antigen.	Complement, 1 in 10 dil.	Amboceptor, 1 in 1000 dil.	Corpuscles, 5 % susp.	Result.
I	0.1 c.c.	0.2 c.c.	0.5 c.c.	1 c.c.	1½ c.c.	No hemolysis.
II	0.1 c.c.	0.2 c.c.	0.9 c.c.	1½ c.c.	1½ c.c.	No hemolysis.
III	0.1 c.c.	0.2 c.c.	1.3 c.c.	1½ c.c.	1½ c.c.	Complete hemolysis.

In reporting the result of the reaction, most workers employ plus signs to indicate various percentages of inhibition of hemolysis, as 1 +, 2 +, 3 +, and 4 +, the last meaning absence of hemolysis or absorption of all the complement used. Obviously this method does not indicate the strength of the reaction beyond absorption of one hemolytic dose of complement, and takes for granted that all so-called 4 + reactions are of equal strength. The erroneous assumption that treatment fails to affect the strength of the reaction in many cases of syphilis is due largely to the fact that the sera have been repeatedly found to give complete inhibition of hemolysis by this method in spite of vigorous treatment. By testing these sera during the period of treatment with several units of complement, a gradual reduction in the number of units absorbed will usually be found, even though there remain fixation of one hemolytic dose of complement. (See Table III).

Instead of employing the plus signs, we prefer to designate the reactions as negative, weakly positive, medium positive, and strongly positive, up to one unit of complement fixation, and give the number of complement units absorbed in reactions stronger than this. We believe that this method of reporting results conveys more information, as a rule, to the clinician than the plus signs. Acknowledgements are due to Dr. John L. Laird for the principles followed in quantitative determination.

Various means have been described for measuring the percentage of hemolysis in reading the results of the Wassermann reaction. We do not believe that accurate estimation of the amount of hemolysis is of importance in the majority of cases, nor can this be done by the eye alone. Yet those who employ the plus signs base their reports upon the percentage of hemolysis as measured by the eye. For those who lay stress upon the accurate measurement of hemolysis in this connection, a method employing the Dubosq colorimeter described by one of us (Ivy)² may be found useful.

A common cause of disagreement in results by different workers is the employment of various substances as antigens, ranging from crude alcoholic extracts of syphilitic and normal tissues, to various synthetic products formed by complicated processes. Wassermann and his followers for a long time clung to the belief that the syphilis reaction was a true antigen-antibody reaction, between the *Treponema pallidum* on the one hand and a specific substance produced by it in the patient's blood on the other. They were forced to modify this position by the discovery that alcoholic extracts of normal tissues, such as guinea-pig and human heart, could likewise be employed as antigens with approximately the same results. Nevertheless, it is still held by Wassermann's followers that tissues rich in spirochetes, are superior as antigens to

² Jour. Amer. Med. Assoc., August 10, 1912.

non-syphilitic tissues or synthetic products, and give the most reliable results in routine clinical diagnosis. We adhere to this view as the result of the use of syphilitic liver extract in over 2200 tests, in which our results have differed in no material way from those of reliable workers. This statement is made after a trial of some cholesterinized extracts of guinea-pig heart and human heart, kindly furnished by Dr. J. A. Kolmer, who with Casselman has recently reported favorably as to their reliability somewhat to the disadvantage of the syphilitic liver extract, in a paper read before the Pennsylvania State Medical Society, September, 1913. Walker and Swift³ also claim a higher percentage of positive results for cholesterinized extracts of normal organs than for alcoholic extracts of syphilitic liver. These extracts are made by adding cholesterin to the crude alcoholic extract of normal heart in a strength of 0.4 per cent. The cholesterinized guinea-pig heart extract was used by us along with our own antigen of alcoholic extract of syphilitic fetal liver in the routine examination of 100 cases, the cholesterinized human heart extract being employed in 33 cases. These investigations covered a period of several weeks. We may say that the differences in results with the three antigens were no more marked at the end of the period during which these comparative tests were made than at the beginning, so that they cannot be ascribed to deterioration of the extracts. Careful titration of the antigens was carried out before doing the tests, and at no time was more than one-third of the anticomplementary dose used. The comparative results with syphilitic liver extract and cholesterinized guinea-pig heart extract may be divided into four groups as follows:

1. In 22 cases the results were positive with both antigens, and showed little or no difference in the degree of reaction.
2. In 8 cases the syphilitic liver extract gave a weakly positive reaction, while the cholesterinized extract gave a stronger reaction.
3. In 36 cases both antigens gave a negative result.
4. In 34 cases the syphilitic liver extract gave a negative reaction, while the cholesterinized heart extract gave a weakly positive or medium positive result. This is naturally the most important group from the clinical stand-point, 9 of these 34 cases were treated cases of syphilis exhibiting no symptoms, showing that it is more difficult to render the serum negative to the cholesterinized extract by antisyphilitic treatment than to the syphilitic liver extract. The remaining 25 of this group were cases submitted for diagnosis or who had no signs or history of syphilis. Where one antigen reacted more strongly than the other, it was always the cholesterinized heart extract. In no case did the syphilitic liver extract give a stronger reaction than the cholesterinized extract.

In the comparative tests with the cholesterinized extract of human

³ Jour. Exper. Med., July, 1913

heart, of 33 cases there were 6 in the first group, *i. e.*, equally positive with the two extracts; 4 in the second group, in which the cholesterinized extract gave a distinctly stronger reaction than the syphilitic liver antigen; 16 in the third group, in which both antigens gave negative results; 7 in the fourth group, which were negative with the syphilitic antigen, but positive with the cholesterinized heart extract.

In the first series, therefore, the results with the two antigens disagreed in 42 out of 100 cases, and in the second series in 11 out of 33 cases. We see from this that the cholesterinized extracts gave apparently a more "delicate" reaction than the extract of syphilitic liver, but we also found that many weakly positive results were obtained by the former in non-syphilitic cases. This last fact alone is quite sufficient in our opinion to offset any advantage in delicacy of the reaction obtained with the use of cholesterinized extracts. We feel that just as high a percentage of positive results is obtained in known or clinically apparent syphilitics with a good syphilitic liver extract as with the cholesterinized antigens, and we do not get positive results with non-syphilitic sera. This is doubtless due in part to the use of one unit of complement and amboceptor properly standardized as described above, instead of double or triple units as employed by many workers. We must conclude that with cholesterinized antigens, weakly and medium positive, and occasionally strongly positive reactions, may be obtained in many conditions other than syphilis, and in normal persons. While our experience with the use of cholesterinized extracts is limited, and we have no criticism to make of the commendable experimental studies being carried on for the improvement of the Wassermann technique, we regard the employment of these artificial antigens for routine clinical use at the present time, instead of being an advance in serological technique, as a distinct step backward. Schamberg, Kolmer, Ringer, and Raiziss⁴ report that they obtained positive Wassermann reactions using the cholesterinized antigens in over 28 per cent. of 22 cases of psoriasis, in several of which syphilis could almost certainly be excluded, thus providing evidence that weak reactions with these antigens do not necessarily mean syphilis, and that only strong reactions with them should be reported as positive. Kolmer and his associates⁵ state that 10 per cent. of normal sera may yield weak positive reactions with cholesterinized extracts. If therefore the results of the reaction with these extracts cannot be relied upon in a considerable percentage of cases, we see no advantage of employing them along with syphilitic liver extract. We claim that with syphilitic liver extract, using the technique described, weakly positive reactions mean nothing else but syphilis. Even granting for a moment

⁴ Jour. of Cutan. Dis., October, 1913.

⁵ Arch. Int. Med., December, 1913.

that the cholesterinized antigens give a more delicate reaction and may furnish positive results occasionally in cases of syphilis that are negative to the syphilitic liver extract, it is a very much less serious error to overlook an occasional case of syphilis, than to saddle a diagnosis of the disease, with all it entails, upon a patient who does not have syphilis. Considerable harm is being done at the present time by the use of unreliable non-specific or artificial extracts, in two ways: (1) The marked discrepancies between the results of the Wassermann test and the clinical findings in many cases are causing sceptical clinicians to lose confidence in the value of the reaction, and thus they are being deprived of an important diagnostic and therapeutic aid; (2) a great many unfortunate people are being treated for syphilis who have not and who never had syphilis, as the result of weakly positive and doubtful reports by workers using these antigens.

It seems to the writers that there should be some means of coöperation of Wassermann workers for standardization and uniformity of methods, to be adhered to as long as they are justified by clinical results, with the acceptance from time to time of such advances in technique as may be approved. In this way only will the serological syphilis reaction retain the confidence that its intrinsic value merits.

THE INVOLUTION OF THE NASOPHARYNX, AND ITS CLINICAL IMPORTANCE.

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NEW YORK.

THE vulnerability of the nasopharynx—that gateway of almost all human diseases—is due to three causes: man's assumption of an upright position, the growth and development of the brain, and the retrograde metamorphosis of the nose, face, and teeth of man.

Too much emphasis cannot be laid on the facts that almost all diseases are air-borne; that the particles which carry the disease pass through the air to the recipient; that this passage is made comparatively easy because of an exposed and unprotected part of the air tract; that the bacteria, whether they come from the mouth or through the nose, cling to this unprotected spot, develop here, and thus the disease begins. This unprotected spot is the nasopharynx; therefore, clinically, the care of the nasopharynx is of supreme and inestimable importance.

The reasons for our estimate of the supreme importance of the nasopharyngeal region are:

1. In many diseases, the primary symptom is found in this locality.

2. The secondary symptoms are traceable from the nasopharynx.

3. The management of the nasopharyngeal region controls the distant manifestations of the disease.

4. The individual's immunity from disease is in direct proportion to the resistant power of the nasopharynx.

5. Man is more subject to air-borne diseases than quadrupeds.

The reason for this is that in quadrupeds the nasopharynx has no unprotected spot. In general, the infections of animals gain entrance through the alimentary tract or skin, whereas with men infections enter through the air tract.

Clinically, primary affections of the larynx, trachea, and lungs form an extremely small proportion of the affections of the air tract. Therefore the great bulk of infections must take place through the upper air tract. The nose is known to be extremely resistant to infections; this is fortunate, as the nose serves as the outpost and occupies a most exposed position. The oropharynx is of more importance, and to it can be ascribed a number of primary infections. But we do not find the portal of entry of the bulk of infections until we reach the nasopharynx. And we find it there because in the nasopharynx is an unprotected spot which, while it becomes a culture medium for bacteria, furnishes a gateway for the entrance of the infection into the individual.

The question naturally arises: Why does Nature, that great protector, leave this space in man unprotected? The comparative study of the evolution of vertebrates explains this. The assumption of the erect position of man has left this spot without the protection of the peristaltic tube which is found in this region in quadrupeds. The erect position brings the foramen magnum and the vertebral column from a position at the posterior aspect of the skull to a position at the inferior aspect of the skull. The base of the skull is bent to give a larger area for the convexity of the brain; and the facial bones are shortened in connection with the involution of the nose, teeth, and face, thereby bringing the hard palate back close against the vertebral column. In other words, in quadrupeds the attachment of the neck is at the back of the head, and the nose and nasopharynx form a straight tube.

The elevation of man to the erect position without disturbing the orientation of his labyrinth or eye planes would have necessitated a right-angle bend in his neck had not the attachment of his vertebral column been changed from the posterior aspect of his skull, as in quadrupeds, to the inferior aspect which it now occupies. Meanwhile, the growth of man's brain required change in the configuration of the base of his skull, namely, the sphenobasilar angle formed between the plane of the upper surface of the basilar process of the occipital bone in the posterior cranial

fossa and the plane of the superior surface of the sphenoid bone between the lesser wings in the anterior fossa of the skull measured in the median line. This angle varies, forms a straight line (0 degrees) in the opossum to an angle of 75 degrees in man.

These three changes at the base of the skull encroached upon the nasopharynx, bending it until it now forms a right angle. The angle referred to is the right angle opening forward and downward, formed by the bodies of the two upper cervical vertebræ and the basilar process. This angle is the "dead" or unprotected spot in the nasopharynx. This angular area is unprotected because of its configuration. Since the vertebral column has pushed forward and the hard palate has pushed backward the nasopharynx has lost the power which it had in quadrupeds of contracting and cleaning itself by peristaltic action. Instead of the abundant ciliated epithelium found in this vicinity in quadrupeds, in man there is only a small amount of imperfectly developed ciliated epithelium next to the choanæ.

The lack of protection in this non-collapsible cuboid space is the reason why the air tract is the most susceptible region of the body; why the upper air tract is the weakest part of the air tract; why the pharynx is the least resistant region of the upper air tract; why the nasopharynx is the part of the pharynx most liable to infection; why the first tonsillar region is the most assailable part of the nasopharynx; and why the angle in the first tonsillar region is the most vulnerable point in the first tonsillar region, and therefore in the whole body.

The epithelial lining of the nasopharynx is tall, columnar, ciliated epithelium near the nasal boundary, and stratified squamous epithelium in other parts, with a variable intermediate region of non-ciliated columnar epithelium. The walls of the nasopharynx are generously supplied with lymphoid tissue. This lymphoid tissue, which is spread over nearly the whole of the walls of the nasopharynx, is very much thickened over the central and posterior part of the vault of the nasopharynx, forming several parallel sagittal ridges, with a deep sulcus in the median line. This mass of lymphoid tissue forms the two lobes of the tonsil of Luschka, or first tonsil. The pharyngeal bursa lies between the lobes of the first tonsil.

This mass of adenoid vegetation is found in a corner formed by the bending of the posterior pharyngeal wall at the angle of the nasopharynx. Here the respiratory current is bent at right angles, necessarily forming eddies, and thus providing a place where the air current slows down, favoring the lodgement of floating particles.

The angle is the point where the momentum of the floating particles and the slowing down of the air current favor their sticking to the wall. At this place, also, the ciliated columnar epithelium continuous with the ciliated epithelium of the nose changes into

non-ciliated pavement epithelium. This epithelium, since it has lost the cleansing power of the peristaltic collapsible nasopharynx of the quadruped, has no means by which to free itself from foreign material except through the uncertain flow of mucous secretions.

The oropharynx is provided with many strong muscles which act in coördination in peristaltic contraction of the oropharyngeal tube during the act of swallowing, thus squeezing out and carrying off adherent mucus and foreign material. The upper limit of this peristaltic tube is the soft palate.

The soft palate, when contracted, forms a diaphragm between the oropharynx and nasopharynx in man. The nasopharynx lies above the soft palate and the peristaltic tube which the soft palate forms with the oropharynx, and consequently the nasopharynx cannot be cleaned by muscular contraction. The nasopharynx is therefore dependent upon its ciliated epithelium to keep it clean, and to the flow of excreted mucus to wash off foreign material from the pavement and columnar epithelium lacking in cilia.

Just in this region, at the point of the bending of the respiratory current, between where the esculator takes up its burden and where the tube conveyer commences—that is, between these two mechanisms—is located the general dump, cleaned only by a precarious flow of mucus. This general nasopharyngeal dump is at the point where the “adenoid” is located. This locality, on account of its lack of protection, serves not only as the point of entry for bacteria, but also as a culture medium, where the bacteria can develop almost without hindrance. The virulent toxins which they produce may cause disturbances at distant points.

The pharyngeal tonsil, or first tonsil, appears from its position to be mechanically the most vulnerable point in the air tract, and if in the air tract, then in the body. A mass of lymphoid tissue protects it and probably serves as a barrier to the entrance of infectious organisms. Infections of the upper air tract occur oftenest in Waldeyer's ring, and in the pharyngeal tonsil more often than in any other part of the ring.

The typical changes in the course of an acute infection through the adenoids are characteristically shown in acute rhinopharyngitis. The onset is expressed by increased secretion, congestion, and swelling of the adenoid. The reaction spreads and increases in violence according to the course of the infection.

A constant characteristic in chronic inflammation, having its origin in the upper air tract, is shown in the swelling, increased secretion, altered blood-supply of the first tonsil, and the conspicuous absence of subjective symptoms.

In the first, or Luschka tonsil, as has been previously recognized in the faucial tonsil, an infection may be localized and very active; or, again, it may be extremely insignificant locally whereas the distant effects acquire a dangerous importance.

AIR-BORNE INFECTIONS. Diseases due to air-borne infections enter the human body in three ways: through the respiratory tract, through the skin, and through the digestive tract. The diseases entering through the nasopharynx are in the maximum both in number and in importance. As scientific observations multiply, significant additions are being made to the list of infections entering through the air tract. This list now comprises the exanthemata, and nearly all diseases due to the local or distant effects of bacterial parasites. The only exceptions are the few diseases caused solely by the entrance of the pathogenic microorganisms directly into the tissue or through the walls of the alimentary canal and genito-urinary tract.

A partial list of affections which may be acquired by means of the inspired air, and many of which are exclusively thus acquired are: the exanthemata; tuberculosis; leprosy; glanders; actinomycoses; syphilis; influenza; infection by pyogenic bacteria affecting brain, cord, ears, nose, and throat, larynx or lungs, and heart; epidemic parotiditis; epidemic cerebrospinal meningitis; epidemic poliomyelitis; rheumatism; lobar pneumonia; bronchopneumonia; coryza; chorea; gastric and duodenal ulcer; arteriosclerosis; functional irregularities of the internal secretions; myxedema, Graves' disease; Addison's disease; acromegaly; pericarditis; myocarditis; endocarditis; asthma; hay fever; lymphadenitis; typhoid fever; purpura hemorrhagica; pertussis; diphtheria; nephritis; meningitis; sinusitis; mastoiditis; appendicitis; leukemia; Hodgkin's disease. All diseases except venereal disease, animal parasites, local intestinal diseases and local skin diseases may be included in the above list of diseases entering by way of the air tract.

CONCLUSION. The number of these primary air-tract infections is so great, and their importance is so overwhelming, that the point of entry of the infection—the nasopharynx—is invested with a spectacularly strategic importance from an etiological and clinical point of view.

METABOLISM STUDIES IN A CASE OF MYASTHENIA GRAVIS.¹

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I. INTRODUCTION. In the normal individual the extent of the consumption of energy is largely dependent upon the conditions of

¹ Read in abstract before the Pittsburgh Academy of Medicine, February 10, 1911.

the muscular system. On this account we would expect to find, when muscular activity and muscular tone are depressed by a pathological condition of the muscle as seen in myasthenia gravis, some changes in the metabolic functions of the body.

II. CLINICAL HISTORY OF CASE. (By Dr. Diller.) The patient is a boy, aged sixteen years, who was first examined for Dr. Diller by Dr. George J. Wright, March 3, 1913. His chief complaints were weakness in the legs, back, and in chewing. This weakness grew much worse with use of the muscles, and he frequently stumbled and fell.

The family history is good. The father and mother and two sisters and brothers are all living and well. The boy himself developed as a hearty, rugged youth, and went to school until two months ago. As a child he had measles, chicken-pox, and smallpox. He has had no acute illness in the past five years, except an attack of tonsillitis, which occurred one year ago.

The present illness began about three months ago, with drooping of the right eyelid. On several occasions he has seen double. About two months ago he noted that he would stumble over any unevenness on the street, and was conscious that his legs were weak. At the same time he noted that his jaw muscles were weak, and that they gave out, especially in chewing anything hard. Afterward he noted that his speech would become more and more indistinct as he talked. He has had no headaches nor pains of any sort. There has been no change in his mental condition.

Examination. The patient is a tall boy, large for his age, weighing 146 pounds. His color is good. There is considerable ptosis of the right lid. The face is smoothed out and expressionless. The pupils are equal, $3\frac{1}{2}$ mm., respond to light and accommodation; no nystagmus. When he makes an effort to look to the left, in the extreme movement, he sees double; but there is no apparent strabismus. The muscles of the face are all weak; the masseters are distinctly weak. He cannot pucker his lips nor make forcible movements, as in laughing. The movements of the arms and legs are all weak, as tested by resistance. The gait is distinctly weak. Dyn. right, 42; left, 34. Several times in dressing and undressing the boy tired out and was compelled to rest. The effort necessary to put on his collar was almost too much for him, and he had to call his mother to his assistance. He quickly tires upon any exertion. After reading aloud a few minutes his articulation becomes indistinct and finally unintelligible. The masseters likewise tire quickly. Indeed all muscles of the body tire readily. The tendon reflexes are all greatly reduced.

No tremors; no atrophies; no sensory changes of any sort. The boy's mind seems perfectly clear.

The boy remained in the hospital about four weeks. After

the conclusion of the experiments made by Dr. Rosenbloom, covering eight days, the boy was given regularly 10 grams calcium lactate; he continues to take this remedy up to the present time (May 15.) He left the hospital after a month's stay, appearing to have made some slight improvement.

April 30, the boy's mother writes: "He does not seem any worse; in fact, I think he seems to be improving slowly. He can swallow better. He is as happy as a lark, and planning what he is going to do when he gets well."



Case of myasthenia gravis. Note general appearance of muscular weakness, especially smoothed-out appearance of face and partial ptosis of right lid. (Kindness of Dr. A. Henrici.)

III. METABOLISM STUDY (By Dr. Rosenbloom). 1. *Review of Literature.* Pemberton² found a marked loss of calcium by the tissues, during a time of nitrogen retention, in a study of a case of myasthenia gravis. He also found that the creatinin excretion was lower than normal, and thinks that myasthenia gravis is a disease of deranged muscular metabolism.

Spriggs³ also found a lessened excretion of creatinin in a case of myasthenia gravis. The uric acid excretion in his case during a period of no fever was normal.

Kaufmann⁴ has studied the effect of muscular work in a case of myasthenia gravis. In the first series the patient had an intake

² AMER. JOUR. MED. SCI., 1910, cxxxix, 816.

³ Quart. Jour. Med., 1907, vii, 63.

⁴ Monats. f. Psych. u. Neurol., 1906, xx, 299.

of 0.24 gram nitrogen and 42.4 calories per kilo body weight. During a period in which the symptoms were slight the patient retained 3.57 grams nitrogen per day; in a period when the patient daily walked about 1000 meters, typical signs of disease appeared and the nitrogen retention amounted to 2.38 grams nitrogen. In the later period, when the condition had practically disappeared, the nitrogen retention amounted to about 4.3 grams per day. When the investigations were repeated and during the first period the patient was supplied with 0.29 grams nitrogen and 48.7 calories per kilo; 4.69 grams nitrogen were retained each day.

In the second period, during which general prostration and ptosis appeared after muscular work, there was a retention of 2.26 grams nitrogen; in the third, during perfectly good health, 5.52 grams. In a third series of observation the intake was only 0.14 grams nitrogen and 4.4 calories per kilo. During the first period there was a loss of 0.28 grams nitrogen, in the second 0.96 grams, and in the third a retention of 2.55 grams daily. The relation between the total nitrogen, urea, and ammonia was as follows: In the days when the patient was well the urea was from 82 to 86 per cent. of the total nitrogen; ammonia-nitrogen, 3.5 to 3.7 per cent. When signs of fatigue appeared the urea was diminished to 62.4 to 74 per cent. of total nitrogen and the ammonia increased to 8.6 to 13.2 per cent. of the total nitrogen.

The high ammonia indicates an increased excretion of acids. He found large quantities of lactic acid in the urine and blood serum on the days of work. In this case, as in the cases of Mohr⁵ and Boldt,⁶ the liver was diseased, and it seemed as if the appearance of the myasthenia coincided with the extent of the formation of the intermediary products of metabolism. Kaufmann also estimated the creatinin on two days, finding it very low; but his results cannot be considered accurate, as the zinc chloride method was used. Spriggs could not detect any increase of lactic acid in the blood in the case of myasthenia gravis studied.

From the work of Loeb and others we know that the calcium ion plays an important part in normal muscular action, and on account of this fact, and the finding of Pemberton of a marked loss of calcium in a case of myasthenia gravis, we paid special attention to the calcium metabolism of our patient.

Folin has suggested that the creatinin output on a meat-free diet in any individual is a constant, independent of muscular work, and is an expression of the endogenous cellular metabolism. Shaffer believes the urinary creatinin is the result of some special process of normal metabolism, which takes place to a large extent, if not entirely, in the muscles, and that the amount of creatinin

⁵ Berl. klin. Woch., 1903, No. 46.

⁶ Monats. f. Psych. u. Neurol., 1906, xx, 39.

in the urine, expressed in milligrams per kilo of body weight, is an index of this special process, and claims that the muscular efficiency of the individual depends upon the intensity of this process. He found that normal individuals excreted between 7 to 11 milligrams of creatinin-nitrogen per kilogram of body weight. Spriggs believes urinary creatinin is a product of the internal structural metabolism of muscle and not of its contraction. On account of the interest in the creatinin excretion of individuals suffering from muscular disease, we also included in our study the excretion of creatinin and creatin by our patient.

2. *Metabolism Methods.* During the entire experiment upon our patient he received daily the Folin⁷ diet, consisting of:

Whole milk	500 c.c.
Cream	300 c.c.
Eggs (whole)	450 gm.
Horlick's malted milk	200 gm.
Sugar	20 gm.
Salt	6 gm.
Distilled water (about)	2000 c.c.

From the fourth to eighth day of the metabolism experiment about 300 grams of egg-yolk was added to the above diet, hoping that if this patient was losing calcium the increased phosphorus intake might cause a retention of calcium. The mixture was prepared fresh every day, and portions taken out for analysis. The ammonia, total nitrogen, urea, creatin, and creatinin were estimated in the fresh urine, but the other constituents were estimated at the end of the experiment. The feces were marked off by means of carmine into periods of two days.

(a) *Methods Used in Urine Analysis.* The nitrogen was estimated by the Kjeldahl method. The ammonia by the Folin⁸ method. The total sulphur by the Benedict⁹ method. Total and ethereal sulphates by the Folin¹⁰ method. The inorganic sulphates computed by subtracting the ethereal sulphates from the total sulphates and the neutral sulphur by subtracting the total sulphate-sulphur from the total sulphur. Urea was estimated by the Benedict¹¹ method. Total phosphorus by the Neumann¹² method, weighing the phosphorus as magnesium pyrophosphate. Creatinin and creatin by the Folin¹³ method. Uric acid by the Krüger-Schmidt¹⁴ method. Calcium and magnesium by the McCrudden¹⁵ method.

⁷ Amer. Jour. Phys., 1905, xiii, 45.

⁸ Zeit. f. physiol. Chem., 1902, xxxvii, 161; Amer. Jour. Phys., 1903, viii, 330.

⁹ Jour. Biol. Chem., 1909, vi, 363.

¹⁰ Amer. Jour. Phys., 1905, xiii, 51; Jour. Biol. Chem., 1906, I, 131.

¹¹ Jour. Biol. Chem., 1911, viii, 405.

¹² Zeit. f. physiol. Chem., 1902, xxxvii, 129; 1904, xliii, 35.

¹³ Amer. Jour. Phys., 1905, xiii, 45.

¹⁴ Zeit. f. physiol. Chem., 1905, xlv, 1; Jour. Biol. Chem., 1908, vii, 27.

¹⁵ Jour. Biol. Chem., 1911, x, 187.

(b) *Methods Used in Analysis of Food.* Nitrogen by the Kjeldahl method. Total sulphur by the Wolff and Osterberg¹⁶ method, a modification of the Benedict method. Calcium and magnesium by the McCrudden method after ashing and extracting the ash with hydrochloric acid. Phosphorus by the Neumann method. Fat was estimated in two-day periods by extraction in Soxhlet apparatus.

(c) *Methods Used in Analysis of Feces.* Nitrogen by the Kjeldahl method. Sulphur by oxidizing with fuming nitric acid followed by the Benedict method. Phosphorus, calcium, and magnesium were estimated by the same methods as used for the food. Fat by the Kumagawa and Suto method.¹⁷

DISCUSSION OF TABLE I. It is of great advantage to use the Folin diet in metabolism experiments, as Folin in his fine investigations on the composition of normal urines has given us the means whereby we can compare the results obtained in diseased states, with his normal values, thereby facilitating the explanation of pathological findings. This diet is a purin-free diet, consisting of about 119 grams protein, 148 grams fat, and 225 grams carbohydrate.

It may be noted that in the last six days of the experiment the patient lost 3.6 grams nitrogen. The relation of the urea-nitrogen and ammonia-nitrogen to the total nitrogen is normal in character, showing no acidosis was present. The creatinin excretion is definitely less than normal, while the creatinin-coefficient is just about one-half the normal. This finding seems to point to the fact that myasthenia gravis may be a disease of deranged muscular metabolism.

The uric acid excretion both in amount and in relation to the total nitrogen is below normal. The amount of undetermined nitrogen excreted in the urine is normal. The protein absorption as deduced from the amount of nitrogen in the feces was also normal.

In this case of myasthenia gravis there is no doubt that the true cellular or "endogenous" metabolism is not proceeding along normal lines, as both the uric acid and creatinin excretion are much lower than normal, two constituents of urine, which form a good criterion as to the extent of the cellular metabolism. The finding seems to emphasize the necessity of considering myasthenia gravis as a disease of deranged muscular metabolism.

The accompanying tables contain the data obtained in this study:

¹⁶ Bioch. Zeit., 1910, xxix, 429.

¹⁷ Ibid., 1908, ix, 337.

TABLE 1.—The Nitrogen Metabolism and Urinary Nitrogen Partition.

Date, 1913.	Urine. ¹⁸										Feces							
	Urea-nitrogen.			Ammonia.			Creatinin ¹⁹			Uric acid.			Undetermined nitrogen.			Nitrogen.		
	Volume, c.c.	Total nitrogen, grams.	Grams.	Total nitrogen, per cent.	Grams.	Nitrogen, per cent.	Grams.	Nitrogen, per cent.	Total nitrogen, per cent.	Grams.	Nitrogen, per cent.	Total nitrogen, per cent.	Grams.	Nitrogen, per cent.	Total nitrogen, per cent.	Nitrogen intake, per cent.	Nitrogen intake, grams.	Nitrogen balance, grams.
March 14	920	16.5	13.7	83.0	0.76	0.63	3.8	1.14	0.42	2.5	0.48	0.16	0.98	1.60	7	14.9
March 15	1070	16.5	13.7	82.8	1.21	0.99	6.0	0.81	0.30	1.8	0.46	0.15	0.91	1.36	8.3	15.6
March 16	2000	16.8	14.1	84.0	0.92	0.75	4.5	1.24	0.46	2.7	0.45	0.15	0.89	1.33	7.9	15.4	-3.50	-3.50
March 17	1380	17.2	14.4	83.6	0.86	0.71	4.1	1.46	0.54	3.1	0.49	0.16	0.93	1.39	8.1	20.6	+1.30	+1.30
March 18	1140	17.0	14.3	84.2	0.85	0.70	4.1	1.21	0.45	2.7	0.43	0.14	0.83	1.41	8.3	20.2	+0.40	+0.40
March 19	2140	17.3	14.7	85.1	0.68	0.56	3.3	0.96	0.36	2.1	0.39	0.13	0.75	1.55	8.9	19.8	-0.30	-0.30
March 20	1650	16.9	14.2	83.8	0.71	0.59	3.5	1.33	0.49	2.9	0.37	0.12	0.71	1.50	8.8	23.1	+3.10	+3.10
March 21	1900	17.0	14.4	84.5	0.87	0.72	4.2	0.96	0.36	2.1	0.42	0.14	0.82	1.38	8.1	15.5	-4.60	-4.60

¹⁸ No creatin was present in the urine at any time.¹⁹ Average creatinin coefficient, 6.3 milligrams per kilo of body weight.

Average creatinin excretion, 1.04 grams per day.

Average creatinin-nitrogen excretion, 0.42 gram, or 2.5 per cent. of the total nitrogen excretion.

TABLE II.—The Sulphur Metabolism and Urinary Sulphur Partitions.

Date, 1913.	Urine.										Feces.		
	Sulphur, grams.	Sulphate sulphur.		Ethereal-sulphate sulphur.		Inorganic sulphate sulphur.		Neutral sulphur.		Sulphur, grams.	Sulphur intake, grams.	Sulphur balance, grams.	
		Grams.	Total sulphur, per cent.	Grams.	Total sulphur, per cent.	Grams.	Total sulphur, per cent.	Grams.	Total sulphur, per cent.				
March 14	1.27	1.15	90.5	0.15	11.8	1.00	78.7	0.12	9.4	1.6	
March 15	1.30	1.16	89.2	0.20	15.4	0.96	73.8	0.14	10.8	1.6	
March 16	1.52	1.40	92.1	0.19	12.5	1.21	79.6	0.12	7.8	0.38	2.2	+0.30	
March 17	1.36	1.30	95.6	0.10	7.3	1.20	88.3	0.06	4.4	0.38	2.2	+0.46	
March 18	2.12	1.98	93.4	0.35	16.5	1.63	76.9	0.14	6.6	0.42	2.0	-0.54	
March 19	2.08	2.00	96.1	0.18	8.6	1.82	87.5	0.08	3.8	0.42	2.0	-0.50	
March 20	1.87	1.72	91.9	0.12	6.4	1.20	85.5	0.15	8.0	0.45	2.1	-0.12	
March 21	1.45	1.30	89.6	0.15	10.3	1.15	79.3	0.15	10.1	0.45	2.0	+0.10	

TABLE III.—The Calcium, Magnesium, and Phosphorous Metabolism.

Date.	Urine.			Feces.			Intake.			Balance.		
	Phosphorous, grams.	Calcium oxide, grams.	Magnesium oxide, grams.	Phosphorous, grams.	Calcium oxide, grams.	Magnesium oxide, grams.	Phosphorous, grams.	Calcium oxide, grams.	Magnesium oxide, grams.	Phosphorous, grams.	Calcium oxide, grams.	Magnesium oxide, grams.
March 14	0.45	0.14	2.2	0.10	2.6	1.8	0.32	-0.85	+0.08
March 15	0.48	0.15	2.4	0.10	2.6	1.8	0.32	-1.08	+0.07
March 16	1.31	0.60	0.15	1.4	2.1	0.12	2.4	1.9	0.37	-0.31	-0.80	+0.10
March 17	1.62	0.91	0.16	1.4	2.3	0.12	4.8	1.9	0.37	+1.06	-1.31	+0.09
March 18	1.90	0.56	0.20	1.6	2.0	0.15	5.12	2.6	0.44	+1.70	+0.04	+0.09
March 19	1.94	0.59	0.21	1.6	2.4	0.15	5.4	2.6	0.44	+1.86	-0.39	+0.08
March 20	1.98	0.95	0.20	1.9	2.6	0.14	5.5	2.8	0.43	+1.62	-0.75	+0.09
March 21	1.92	1.16	0.19	1.9	2.8	0.14	4.5	2.8	0.43	+0.68	-1.16	+0.10
Totals	10.67	5.70	1.40	9.8	18.8	1.02	28.6	12.2	3.12	+6.61	-6.3	+0.70
Averages	1.78	0.71	0.175	1.6	2.35	0.13	3.6	2.3	0.39	+1.10	-0.8	+0.087

DISCUSSION OF TABLE II. During the last six days of the experiment the patient shows a slight loss of sulphur. The amount of sulphur excreted as ethereal sulphate and as inorganic-sulphate is normal in character. The amount of neutral sulphur excreted in relation to the total sulphur is below normal. This finding also substantiates our idea that myasthenia gravis is a disease of deranged muscular metabolism, as Folin also claims that the neutral sulphur of the urine represents a partial expression of the endogenous or cellular metabolism, in the same manner as does the creatinin and uric acid excretion. As is well known, these three constituents of the urine are the truest index to the so-called "endogenous" metabolism of an individual. In this disease, we have therefore a low "endogenous" metabolism, and if it is true that the "endogenous" metabolism initiates and directs

the processes of cell life, we have a further proof for our idea that myasthenia gravis is a disease due to some metabolic perversion. It might be possible that the lack of utilization of the calcium ion prevents the "endogenous" metabolism proceeding in a normal manner.

TABLE IV.—Calcium Oxide and Magnesium Oxide Output.

Day.	Calcium oxide in urine, per cent.	Calcium oxide in feces, per cent.	Magnesium oxide in urine, per cent.	Magnesium oxide in feces, per cent.
1 .	16.9	83.1	58.3	41.7
2 .	16.6	83.4	60.0	40.0
3 .	22.2	77.8	55.5	44.5
4 .	28.3	71.7	57.1	42.9
5 .	21.9	78.1	57.1	42.9
6 .	19.7	80.3	58.3	41.7
7 .	26.7	73.3	58.8	41.2
8 .	29.2	70.8	57.6	42.4

DISCUSSION OF TABLES III AND IV. In this case of myasthenia gravis we have found a marked loss of calcium by the tissues, 6.3 grams calcium oxide in eight days, thereby confirming the findings of Pemberton. However, during a time of phosphorus retention produced by the feeding of egg-yolk, no effect was noted on the calcium metabolism.²⁰

A slight retention of magnesium was found, + 0.7 gram, during the eight days. On account of the great importance that the calcium ion plays in normal muscular action, it is tempting to think that possibly it is owing to some lack of utilization of this substance that the condition of myasthenia gravis owes its origin and that the changes we have observed in the "endogenous" or cellular metabolism in this disease may be secondary to this fact and as it has long been known that the inorganic ions are necessary for normal muscular action, as a hypothesis we might say that it is owing to some disturbance in metabolism of these substances, especially calcium, that the muscular symptoms of myasthenia gravis are due. We also know that during the work of muscle, lactic acid is produced, one of the factors in the production of fatigue of muscle. May it not be that owing to the fact that the calcium not being utilized normally, the lactic acid is not neutralized by the calcium and fatigue comes on readily, one of the characteristic features of myasthenia gravis? It must also be remembered that any perversion of calcium metabolism may give rise to symptoms in two ways, first, symptoms due to the loss of the calcium, and second, symptoms due to the excess of the other bases. A direct way to attack this problem would be to

²⁰ Loeb (Int. Beitr. z. Path. u. Ther. d. Ernähr., 1911, iii, 237) has also found that a phosphorus retention produced by feeding lecithin, was not accompanied by a calcium or magnesium retention.

devise some method to cause these patients to retain calcium and see if this retention had any favorable effect on the disease.²¹ The distribution of oxide and magnesium oxide in the feces and urine (Table IV) may be considered normal.²² The fat metabolism in this patient (Table V) is also normal in character. In connection with the possible influence that internal secretory organs may have on calcium metabolism, it should be remembered that many have found in myasthenia gravis some disease of the thymus.²³ It is possible that other secretory organs may exert some influence on calcium metabolism. McCrudden²⁴ found that improvements in the symptoms of osteomalacia, following castration, was accomplished by calcium retention, where there had been a loss before. Also, it has been found, that injections of epinephrin²⁵ have been of value in osteomalacia and in rickets. Carnot and Slavu²⁶ have shown that after injection of dogs subcutaneously with epinephrin, that ossification is much greater than in the controls. Quest²⁷ and also Stoltzner²⁸ have studied the effects of epinephrin administration in rickets in relation to the calcium metabolism. Parhan²⁹ has studied the influence of thyroid principle on calcium metabolism in rabbits, showing that ingestion of thyroid determined a loss of calcium from the tissues, which ran parallel to the amount of thyroid ingested.

TABLE V.—The Fat Metabolism.

Date, 1913.	Fat content of feces,		Fat intake, per cent.	Fat intake, grams.	Fat balance, grams.	Fat absorbed, per cent.
	grams.					
March 14
March 15	13.5	10.0	135	+121.5	90.0	
March 16	14.5	10.0	145	+130.5	90.0	
March 17	19.4	10.2	198	+178.6	89.8	
March 18	21.1	10.2	215	+193.9	89.8	
March 19	20.3	10.1	205	+184.7	89.9	
March 20	20.6	10.1	208	+187.4	89.9	
March 21	22.8	9.2	210	+187.2	90.8	

Basch³⁰ has found that thymectomized dogs in comparison with controls of the same litter, revealed lessened growth, less consistency of the bones, and a changed psychical nature, two to three

²¹ I hope soon to study this problem, especially the effect of various internal secretory products on the metabolism of calcium in health and disease.

²² For list of ratio of the urinary and fecal calcium output in normal and pathological conditions, see Towles, *AMER. JOUR. MED. SCI.*, 1910, cxi, 100. For magnesium oxide, see Renvall, *Skand. Arch. f. Physiol.*, 1904, xvi, 94.

²³ Mandelbaum and Celler, *Jour. Exper. Med.*, 1908, x, 808.

²⁴ *Amer. Jour. Physiol.*, 1905, xiv, 211; 1906, xvii, 211.

²⁵ Bossi, *Centralbl. f. Gynäk.*, 1907, Nos. 3 and 6; 1907, xxxi, 1560; Stocker, *Corr.-Bl. f. Schweiz. Aerzte*, 1909, xxxix, 433.

²⁶ *Compt.-Rend. Soc. Biol.*, 1910, lxviii, 832.

²⁷ *Zeitschr. expt. Path.*, 1908, v, 43.

²⁸ *Jahr. f. Kinderheilk.*, li, Nos. 1 and 2.

²⁹ *Compt.-Rend.*, 1913, lxxii, 620.

³⁰ *Jahr. Kinderheilk.*, 1906, lxiv, 285; *Wein. klin. Woch.*, 1903, xxxi, 893; *Deut. med. Woch.*, 1913, xxxix, 1456.

weeks following the thymectomy. They also showed an increased irritability of the cerebral cortex and peripheral nerves and that injections of soluble calcium salts brought the irritability back to normal. MacCallum and Voegtlin³¹ and also Erdheim³² have claimed a relation exists between the parathyroid glands and calcium metabolism.³³

THE SERUM DIAGNOSIS OF PREGNANCY AND ITS UNDERLYING PRINCIPLES.

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IN his test for pregnancy, Abderhalden has opened a field which promises perhaps more for scientific investigation and for ultimate practical usefulness than any other present-day line of study. He and his pupils have devoted a great deal of brilliant investigation to the work of animal ferments, and this test for pregnancy, introducing new laboratory methods of almost unlimited possibilities, is the result of these studies. I shall not discuss the great mass of experiments dealing with this subject the results of which have been reported by various investigators within the past two years. It is too early for a critical survey. The exacting details of the method and the principles underlying it must be more thoroughly understood by those who attempt to follow Abderhalden's work before any effort can be made to reconcile results. I shall confine myself to a discussion of these principles and to a brief consideration of the technique.¹

All metabolic processes are in last analysis an expression of ferment activity. Each body cell is armed with ferments designed not only to protect it from foreign invasion, but which enable it to meet its requirements for energy, maintain its structural integrity, and perform its specific functions. The study of these cell ferments, overshadowing in importance everything else in physiology (and perhaps in pathology), is after all still in its infancy, for we know nothing of the exact nature of the chemical composition of ferments, and are forced to recognize them solely by the character of their work.

³¹ Jour. Exper. Med., 1909, ix, 118.

³² Frankfurt Zeitsch. f. Path., 1911, vii, 178.

³³ For review of literature regarding the influence of internal secretory organs on mineral metabolism see Bayliss and Staring, *Erg. d. Physiol.*, v, p. 664; Vincent, *Erg. d. Physiol.*, ix, p. 145; *Internal Secretion and Ductless Glands*, 1912 (Arnold); Oppenheimer, *Hand. d. Biochemie*, 1910, 3, part 1; Biedl, *Innere Sekretion*, 1913.

¹ References to the voluminous literature upon animal ferments have been omitted. This may be found in complete form in Abderhalden's *Abwehrfermente des tierischen Organismus*, Julius Springer, Berlin.

On first thought we should expect to find the studies of ferments simplest among the unicellular bodies. We should expect their metabolic processes to move along simpler lines and to unfold themselves more readily to view. On further consideration, however, it is seen that the metabolic processes of unicellular organisms must necessarily be more complex and more difficult of access than is the case with those organisms in whose construction many kinds of cells are concerned; for with the former, absorption and excretion run parallel, and it is extremely difficult, in fact, impossible, to study in detail their manifold metabolic processes. As we go higher in the animal scale, we find specialized groups of cells, each monopolizing certain functions and gradually losing others. Such cell groups with their special functions we recognize as organs. From this viewpoint we can regard the animal organism as a cell community, each member of which, working for the good of the whole, has its definite duties to perform.

The first attempt at formation of a cell community which we call symbiosis, is seen in that mutual coöperation between unicellular bodies. Here the cells, though separate and distinct, bind themselves together because of a common interest. A little higher up the scale and we come upon the various cell groups of multicellular bodies. When one of these groups has formed an alimentary tract, it alone, as Abderhalden points out, stands in physiological relationship to the outer world. It alone determines for the organism the nature of its absorbed foodstuffs.

The prime object of digestion is to protect the body against the invasion of foreign substances, a recognition of which fact is necessary for a proper understanding of the principles upon which Abderhalden bases his work. No foodstuffs are absorbed directly. Neither proteids, carbohydrates, nor fats undergo immediate absorption, nor can they be reduced directly to their metabolic end-products. Before it is suitable for absorption, each must be broken down to its simplest building stones. This is accomplished by means of ferments produced by the intestinal epithelium and the extrinsic glands. From the mass of amino-acids and other split products thus set free, the organism chooses such building stones as are suitable for use. What immediately follows is shrouded in some doubt. Since amino-acids could not be found in the blood, it was formerly believed that they did not circulate as such, but were united during absorption to form new albumins. Recently, however, Van Slyke and Meyer have found that amino-acids do circulate as such, and in this form are carried to the body cells.

The liver holds up and rapidly destroys any excess of these absorbed bodies. The situation of this organ, between the intestinal epithelium and the body cells, where it can scrutinize and deal with all absorbed substances, is a fortunate one; for it not only aids in

the elaboration of nutritive substances, but also serves as an important defence against foreign invasion. These building stones, perhaps loosely coupled to other substances, are taken up by the muscles and other tissues, and must undergo still further elaboration before they become integral parts of the cell.

Each variety of cell, exhibiting, as we are forced to assume, a structure peculiar to itself, must necessarily select from the materials offered it those building stones which are peculiarly suited to its needs and reject those which it cannot use. This is accomplished by means of cell ferments through digestive processes which are to a certain extent at least identical in nature with those of the alimentary tract. The blood plasma—the source from which each cell draws its building material—is for all cells the same. Consequently we should expect in each kind of cell not only its own specific ferments, but in addition, ferments which are common to all cells. In the study of this, the machinery of the cell, we shall find perhaps “the surest and most direct evidence that cell function is dependent upon cell structure.” Not every split-product thus formed is ready for immediate absorption. At times it must be coupled to some other substance before a satisfactory building stone results. Then follows further coupling of all these manifold building stones until the characteristic complex cell structure is completed.

As an example of such reconstruction, “An architect is directed to construct from a given building which has served a certain specific purpose, and therefore is of special design, another building destined to entirely different uses. He must first demolish the former. From the building stones thus obtained he proceeds along entirely new lines. Many of these are ready for immediate use; others must be reshaped; while still others are wholly unfit. In exactly the same manner the animal organism deals with the complicated cell material coming to it as foodstuffs. First occurs a splitting into the simple building stones, and then beyond the intestinal wall reconstruction follows according to entirely new plans.”

We are accustomed to view ferment activity in too schematic a manner. The conversion by the yeast cell of dextrose into alcohol and carbon dioxide is no doubt a much more complicated process than we ordinarily think, and is probably divided into many intermediary reactions. The meaning to the cell of each of these separate reactions will, as Abderhalden points out, constitute an interesting problem for future investigation, the solution of which will no doubt permit valuable insight into cell metabolism. The cell works step by step, liberating gradually the energy contained in its absorbed substances, and probably never at one stroke converting them to metabolic end-products.

Though every body cell conforms in structure to a certain general

ground-plan common to all, those organ cells which have taken on special functions are distinguished by certain additional peculiarities of structure. We must assume for each variety of cell this specific plan of structure, else how can we explain its specific functions? Certain cells produce specific secretions, and these secretions influence solely cells of a given kind, leaving numberless others untouched. The secretion itself, the cell which produces it, and the cell which feels its influence, must each enjoy a plan of structure peculiar to itself.

With this conception of specific cell structure, and to a certain extent specific cell metabolism, we assume not only that each variety of cell within the human organism possesses its own peculiar build, but also that to a certain extent there is a variation in a given cell between two individuals of the same species. We also recognize that this cell presents still wider variations in structure when derived from animals of different species, and so on down the scale. This demands an infinite variety of structure, while the building stones at our disposal are comparatively few. The following may be quoted to show that our assumption is entirely reasonable: With three building stones we can build six different structures; with four, twenty-four; and with twenty building stones the number of possible structures is 2,432,902,008,176,640,000.

Recent experiments indicate that while the cell albumins of a given organ differ according to the animal from which the organ comes, they at the same time present certain points of similarity. To produce this similarity it is necessary only that there recur always in each of these albumins a given group which, because of certain stereochemical arrangement offers to the specific ferment suitable point for attack. This is important when we come to consider the availability for human experiment of albumins derived from organs of the lower animals.

A striking illustration of the specific adjustment of secretions to cells of a certain structure is cited by Abderhalden in the peculiar condition known as *hermaphroditismus verus*. These peculiar animals possess upon one side an ovary and upon the other a testis, and exhibit upon one-half of the body male and upon the other half female types of development, each stopping sharply at the midline. We must acknowledge that the secretions from each of these glands is brought in contact with all of the cells of both sides of the body; yet each brings to full development the secondary sexual characters peculiar to itself and limits them to its own body half. The secretion from the ovary finds suitable adjustment only in those body cells of the female side, and that of the testis influences only those cells built according to the male ground-plan.

The theory of specific cell structure also finds noteworthy support in the results of transplantation experiments; for heteroplasty has

never proved successful, while tissues which are closely related will usually permit grafting. Pathology furnishes still further evidence in the fact that many poisons, such, for instance, as the tetanus toxin, will attack cells of a certain kind only—those of suitable structure—and leave all others uninjured.

The cell regulates its metabolism in finest detail, both qualitatively and quantitatively, and to accomplish this it must at all times enjoy unchanging conditions in the medium surrounding it. For a given location the composition of the plasma or lymph is always the same. Each cell takes from the plasma the same substances always, and gives to it always the same waste products, and though this fluid maintains for a given point a remarkable constancy of composition, it varies as it passes from place to place in the circulation.

Substances for which the body has use and which properly belong to the organism we call "body-like," while any substance which because of its structure and configuration fails to find adjustment in the organism is termed "body-foreign." Substances belonging to the plasma are "plasma-like," and those belonging peculiarly to the cell we call "cell-like" or "organ-like." Since the albumins of the plasma, as we have seen, must undergo reconstruction before they can become a part of the cell, though plasma-like they can only be regarded as cell-foreign. In like manner, materials belonging to a given cell while cell-like are plasma-foreign; for in the course of normal metabolism they find no opportunity for entering the plasma until through a step by step splitting at the hands of the cell they have been deprived of their specific character. A plasma-foreign substance entering the blood is equally foreign whether it come from the outside world or gain entrance to the plasma through some metabolic error on the part of the cell. The body must recognize it as foreign and deal with it accordingly, no matter what its source.

The animal organism should be regarded as a closed whole. Each organ or group of cells has its own specific duties to perform and contributes its definite part to the general metabolism. Disturb one and the whole machinery is upset. Introduce from the outside some substance which has no place in this general plan, or let some substance from within appear at a place not its own, and the organism feels the shock of foreign invasion.

Invasions by body-foreign for plasma-foreign substances are not uncommon. The bacterial infections and the malignant tumors serve as examples. Abderhalden has asked the question, "What course is open to the cells when body- or plasma-foreign substances gain entrance? Are they defenceless against these substances; or is it possible for the cells beyond the intestinal tract also to break down to harmless bodies such substances and use the building stones thus set free for their own purposes?"

In seeking an answer to this question, it was found that every body cell possesses at least some ferments similar in nature to those of the intestinal tract, and the conclusion is inevitable that these ferments play an all-important role in cell metabolism. It has been found that the body cells are able by means of a hydrolytic process to split fats into alcohol and fatty acids. Carbohydrates undergo similar degradation, glycogen being converted first into dextrin and then into maltose. This last-named is then split to dextrose. Numerous investigators have concerned themselves with inquiries regarding the presence of proteolytic or peptolytic ferments in the tissues. Abderhalden and the writer found no ferments in bovine plasma capable of splitting glycyl-l-tyrosin dl-alanyl-glycin, glycyl-dl-alanin, or diglycyl-glycin; while Abderhalden and Manwaring conducting parallel experiments with red and white cells from the same specimens of blood demonstrated the presence of such ferments. Investigators have almost without exception found peptolytic ferments in the other body cells. No such ferments are found in plasma alone, but there is no doubt that the body cells and the cells of the blood are equipped with ferments capable of digesting albumen.

The question is then asked, "Does the plasma defend itself, against foreign invasion by means of these normal cell ferments, or to meet foreign invasion does it take on new properties?" Experiment shows that the plasma on experiencing the shock of such invasion acquires new ferments—ferments which are specific in action and are directed only against this particular plasma-foreign substance. If cane sugar be added to the serum obtained from a dog, no appreciable change appears within a reasonable time. If, however, the dog first receive intravenously a solution of cane sugar and after a short time the blood be drawn, it will be found that the serum so obtained has the power of converting cane sugar into dextrose. Invertin, the ferment which splits cane sugar, appears in the blood of the dog within fifteen minutes after a solution of this carbohydrate has been injected. Experimenting with the fat tributyrin, it was found that fats also stimulate the production of ferments specific for themselves.

The source of these defensive ferments is yet a matter of conjecture. No doubt all the organs, particularly the intestinal tract, the liver, and the kidneys, play a part, and the lively interest taken by the leukocytes in every form of infection or foreign invasion suggests for them an important role. On the other hand, recent observations indicate that defensive ferments are derived each from the organ against which its activities are directed.

If these facts be true, then it is possible for us to search for plasma-foreign substances by testing the blood-serum for their respective ferments. Upon this Abderhalden bases his test for pregnancy. The placenta, while body-like, is of course plasma-

foreign. Experiment has shown that a living placenta gives off constantly, though perhaps in minute degree, its albumins to the mother circulation. The manner by which this plasma-foreign albumin gains entrance is as yet a matter of doubt. It has been suggested that the cells of the chorionic villi from time to time become dislodged and thus enter the maternal blood. In certain animals, however, the nature of the circulation precludes such an accident. Perhaps at this time of rapid cell activity a certain "overproduction" and "overflow" of a new albumin takes place. In whatever manner this invasion occurs, the mother within the first eight days of pregnancy exhibits in her serum a ferment which is capable of splitting placenta albumin and this only. The blood loses this ferment from fourteen to twenty-one days after the placenta is removed.

Were the practical application of these principles to stop here, Abderhalden's work with the defensive ferments would be of minor importance, since a blood-test for pregnancy is of no great general interest. The field is infinitely broader and richer. Invasion of the organism by body-foreign and plasma-foreign substances is an accompaniment not only of pregnancy but of many pathological states, and if the promise of this work is fulfilled, we shall be able to properly characterize these states—to recognize not only the plasma-foreign substance introduced from without, but also that introduced from within and the organ from which it comes. Through the serum diagnosis of pregnancy we are introduced to the much larger field of the serum diagnosis of organ function. We assume that when one organ becomes diseased or disturbed in function, the altered metabolism causes "unripe" or plasma-foreign albumins to enter the blood. We then test the blood-serum for the resulting specific ferments. It is tested separately against the albumins of all the organs in question, and the particular albumin digested indicates the organ which is diseased.

The opportunities thus opened for studies in physiology and pathology are almost unlimited. In this way the interrelation of the various organs may be studied: the mutual dependence of the organs of internal secretion, degenerations in muscle and nerve, bacterial infections, therapeutic and toxicologic questions, *ad infinitum*. "The whole realm of biology offers no more alluring task than the study of how the organism reacts when the harmony of its metabolism, regulated in finest detail, is disturbed."

Reports of work in this field and suggestions as to modification of technique are appearing in great profusion. The reports from Abderhalden's laboratory and from certain German clinics give wonderfully accurate results in pregnancy and in a variety of diseases. On the other hand, numerous investigators have shown disappointment in their results and express doubt as to the specific action of the ferments. The complexity of the method and the

many pitfalls in the technique warrant always from its adherents the reply that the test was not properly carried out. All agree that before it comes into general use the present method must be changed or simplified, and Abderhalden has recently reported interesting and promising attempts at perfecting a precipitation method which will eliminate the dialysis shells. Certain of my own results have been contradictory, but one fruitful source of error has been discovered in the faulty dialysis shells. I hope to report these studies at another time.

Abderhalden stated recently that over 600 sera in his laboratory had been tested for pregnancy with less than 1 per cent. of error, and that these errors were later shown to have been avoidable. In the same report he tells of over 400 sera from cases of Graves' disease, dementia præcox, carcinoma, sarcoma, tuberculosis, and other diseases which have been tested with startlingly direct and accurate results. Fifty carcinoma sera were diagnosed without an error. In numerous instances serum diagnosis has pointed to certain diseased organs which could not have been recognized clinically.

Notwithstanding the many adverse criticisms, one cannot but recognize that such reports coming from men like Abderhalden, Lampé, and numerous others, cannot be disregarded.

Certain interesting results will serve to illustrate the value of the method. Sera from endemic goitre and myxedema are found to digest thyroid tissue. Exophthalmic goitre serum attacks thyroid, thymus, and frequently the ovary but no other tissue. Dementia præcox serum digests always the ovary or testis and usually the cerebral cortex. It has been reported that serum from patients with miliary tuberculosis will split the tubercle bacillus, and that serum from tuberculous cows splits bovine but not human tubercle bacilli.

Paltauf's case is worthy of mention. He found that a certain malignant tumor from an old woman was not split by known carcinoma serum, but was attacked by pregnancy serum. The microscopic diagnosis proved to be malignant chorioepithelioma.

Just a word regarding the present method. If the precautions prescribed are necessary (and the limited experience of the writer assures him that they are), no one can expect today to obtain satisfactory results who has not thoroughly familiarized himself first hand with Abderhalden's discussion of principles and his elaborate rules as to technique.

Briefly, the principle of the dialysis method of serum diagnosis, the method commonly used, rests upon the fact that colloidal albumin will not diffuse through an animal membrane, while its split products, peptones, and amino-acids, will pass through. The coagulated blood-free tissue of the placenta (or organ in question) is placed in a small dialysis shell, to which is added the serum to be tested. If this serum contains defensive ferments specific

for this tissue, the latter will be digested and its split products will pass through to the distilled water outside the membrane—the dialysate—which after about sixteen hours can be tested with Ninhydrin for these bodies.²

Precautions are numerous and essential. Absolute asepsis in every step is demanded. The dialysis shells themselves must be standardized. They should not permit the passage of albumin, but must all be equally permeable to albumin-split products.³ The preparation of the organ albumins, "substrata," as they are called, must be perfect. When properly prepared and coagulated they are snow-white. They must not contain even the minutest traces of blood or extractive substances. Before it is available for use, each preparation must be tested by the dialysis method for remaining traces of blood. Otherwise, results will be fallacious. All utensils must be in perfect condition both as to cleanliness and asepsis. The water used must be freshly distilled and sterile. Care must be taken to see that uneven evaporation of the different dialysates is impossible.

In applying the Ninhydrin test to the dialysates, the utmost precaution must be observed to obtain in each test identical intensity of boiling. To insure accurate observations as to the resulting color reaction, test-tubes of equal caliber and thickness of wall must be used. The blood-serum must be fresh, and should be actually, not apparently, free of cells. This work should not be done in a laboratory where other chemical or bacteriological experiments are carried out, and a special incubator should be reserved. The author of the method urges that those who undertake it familiarize themselves most carefully with its every detail, and begs that no attempt be made to change the method until we can first analyze our present errors and determine their sources.

And finally as to the part the clinician is to play in these studies. Abderhalden significantly states that physiology has done its part, that it has developed the method and its principles, and that it now remains for the clinician to determine value and scope. He emphasizes the necessity for the most careful clinical study and "follow up" of all cases tested by this method, and urges that patients be carefully classified and studied in large groups or series, rather than as individuals, as only the clinician is competent to do.

I take pleasure in acknowledging my indebtedness for the principles here discussed to the writings of Professor Abderhalden, and particularly to "*Abwehrfermente des tierischen Organismus*."

² The optical method which is less adapted to clinical work depends upon the change in optical rotary power which a mixture of peptones undergoes when subjected to further splitting.

³ The dialysis membranes now being brought on the market, because of the great demand and increased production, are almost universally unsuitable. The only reliable shells known to the writer are those which have been tested in Abderhalden's laboratory. They are sold by Rudolph Shoepfs, Halle, a. s.

THE COMPLEMENT-FIXATION TEST IN TYPHOID FEVER: ITS COMPARISON WITH THE AGGLUTINATION TEST AND BLOOD CULTURE METHOD.¹

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THE diagnosis of typhoid fever has always been a subject for extensive research. In spite of the many laboratory and immunity tests at our disposal (blood culture, agglutination test, leukocyte count and differential, ophthalmo-reaction, cutaneous reaction, diazo reaction, Russo test, cultures of urine, feces, etc.), the clinician is frequently desirous of other corroborative diagnostic methods. When a positive blood culture is obtained, further examinations are unnecessary. A number of our patients, however, come to the hospital after having been ill for some time; at this stage the bacteria are not so frequently detectable in the peripheral circulation. Furthermore, under conditions like too small veins, or inadequate equipment, as is the case out of town, the blood-culture method is less practicable, and the main reliance of diagnosis must be placed upon the Widal test or the leukocyte and differential count. The former is to a certain degree losing in its importance on account of the present favorable tendency toward prophylactic typhoid inoculations, which result in a strong agglutination power of the blood. The possibility of employing the complement-fixation method as a corroborative test in the diagnosis of typhoid fever has been often suggested. The author undertook a systematic investigation of

1. The frequency of its positive finding, its time of appearance and persistence.

2. Its comparison with the agglutination test and blood culture method.

3. Its occurrence after active immunization against typhoid fever.²

1. Bordet and Gengou³ (1901) were the first to demonstrate complement-fixation bodies in the serum from two convalescent typhoid patients; as antigen a saline emulsion of typhoid bacteria grown for twenty-four hours was used. Since then numerous articles referring to this topic have been published, but the conclusions reached are various.

The most favorable reports are by Widal⁴ and Lesourd,⁵ who out

¹ Read at a meeting of the New York Serological Society, October 11, 1912.

² This is the subject of a separate paper in preparation.

³ *Annales de l'Institut Pasteur*, 1901, xv, 290.

⁴ *Compt.-rend. de la Soc. Biolog.*, 1901, liii, 811.

⁵ *Recherch sur la présence d'un sensibilisatrice dans le serum des typhiques*, Thèse, Paris, 1902.

of 61 patients obtained a positive result in 58. They were unable to repeat the test in the 3 negative cases.

Lüdke⁶ examined 30 patients at a time during the acute illness when the temperatures were of the high continuous type and found 7 negative; 14 cases had to be examined twice. He does not therefore attribute much importance to the diagnostic value of the test.

Posner⁷ advises against its introduction because several cases gave a negative reaction, although the Widal test was positive.

Spät and Zupnik⁸ report out of 18 typhoid patients, 11 positive. They found the blood culture more reliable.

Hirschfeld⁹ found positive reactions in all of 15 cases. Undoubtedly this wide difference of opinion is dependent upon variation in the technique of the complement-fixation test, but to the greatest degree upon the preparation of the antigen. Here all possible modifications exist.

The oldest and most reliable antigen is the watery extract of the bacteria, advised by Wassermann and Bruck.¹⁰ This antigen was used with excellent results in the typhoid complement-fixation studies by Hirschfeld,¹¹ Leuchs,¹² and Raskin.¹³

Moreschi¹⁴ as well as Bordet and Gengou¹⁵ used saline suspensions of typhoid bacteria.

Picker's reagent was employed by Van Loghem;¹⁶ Chantemesse's vaccine by Spät and Zupnik.¹⁷ Kentzler and Kiraly¹⁸ prepare an ether extract of the bacteria.

The author's antigen was made according to Wassermann-Citron's¹⁹ directions for preparing artificial aqueous aggressins. Cultures are grown for twenty-four hours upon agar slants or plates (Kolle's flasks are preferable). The growth is washed off with sterile distilled water about 1 c.c. to an agar slant. The total emulsion is kept in a hot-water bath at a temperature of 60° to 65° C. for twenty-four hours, then transferred to a strong bottle and shaken vigorously with the aid of glass beads for twenty-four hours. The bacteria are thus thoroughly broken up. The mixture is next centrifugalized for a long time (four to eight hours depending upon the total quantity) until all the bacteria have sunk to the bottom and the supernatant fluid is absolutely clear. The latter is carefully pipetted off, and can be preserved for about six to eight months in sealed tubes, not exposed to sunlight or room temperature. Sterile precautions must be taken throughout the preparation. The object of using a total small quantity of distilled water is to

⁶ Handbuch, Kraus and Levaditi.

⁷ Berl. klin. Woch., 1908, No. 37.

⁸ Berl. klin. Woch., 1908, No. 40.

⁹ Zeitsch. f. klin. Med., 1907, Band lxi, Heft 3-4.

¹⁰ Med. Klin., 1905, No. 55

¹¹ Loc. cit.

¹² Berl. klin. Woch., 1907, Nos. 3 and 4.

¹³ Centrälbl. f. Bakt., Band xlviii, Heft 4, p. 508.

¹⁴ Berl. klin. Woch., 1906, No. 38, p. 1243.

¹⁵ Loc. cit.

¹⁶ Centrälbl. f. Bakteriöl., Band xlv, Heft 6, p. 190

¹⁷ Loc. cit.

¹⁸ Zeitsch. f. klin. Med., 1908, Band lxx.

¹⁹ Immunity, Methods of Diagnosis and Therapy, Blakiston's Son Co., Philadelphia, 1913.

eliminate the hemolysis of red-blood cells, which may be occasioned by employing large doses of antigen in the test.

It is best to titrate the strength of the antigen about one week after its preparation, as after the end of this period its titer usually remains unchanged. Varying quantities of antigen are mixed with the constant units of complement, hemolysin, and red cells (sheep system), and those amounts are determined which do not of their own accord inhibit hemolysis.

TITRATION OF ANTIGEN.

Typhoid antigen. c.c.	Complement. c.c.	Hemolysin. c.c.	Red blood cells. c.c.	Saline. c.c.	Result.
0.2	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	Up to 2.5	No hemolysis
0.1	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	No hemolysis
0.05	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	Hemolysis complete
0.025	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	Hemolysis complete
0.0125	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	Hemolysis complete
0.00625	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	Hemolysis complete

In accordance with the summation law of Weil and Nakayama,²⁰ the dose of antigen to be employed in complement-fixation experiments is represented by one-half of the maximum quantity of antigen that does not of itself bind complement; that is, in the above instance one-half of 0.05 c.c., or 0.025 c.c., or 0.5 c.c. of a dilution 1 to 20. This unit of antigen is then tested with a known typhoid serum to prove that complement-fixation is possible.

Just as has been demonstrated by Teague and Torrey²¹ and Schwartz and McNeil,²² that for gonococcus complement-fixation work a polyvalent gonococcus antigen is necessary, and by Austrian²³ that for the typhoid ophthalmo-reaction a highly polyvalent typhoid extract is essential, so is it also of fundamental importance, in order to obtain the greatest number of positive results with the typhoid complement-fixation experiments, to have an antigen prepared from a large number of different typhoid strains. The writer is absolutely convinced of this fact. The following case proves this:

Richard, aged nine years, was admitted to the medical service of Dr. Hensel at the German Hospital in August, 1912. Probable diagnosis was typhoid fever. The blood culture disclosed bacillus typhosus, the Widal test in dilution 1 to 50 was positive in one-half hour, but the complement-fixation test was negative. It was repeated several times at intervals of a week, but remained negative. The fourth time (during the convalescence) the reaction was only doubtful. This finding seemed exceptional in comparison with the other results. An antigen was therefore prepared from the patient's own typhoid strain; the complement-fixation test performed with his own extract was strongly positive, and with

²⁰ Münch. med. Woch., 1906, No. 21.

²² AMER. JOUR. MED. SCI., May, 1911.

²¹ Jour. Med. Res., 1907, No. 17.

²³ Johns Hopkins Bulletin, January, 1911.

the stock antigen prepared from seven different strains was doubtful; thus:

Stock antigen.	Patient's serum.	Complement.	Hemolysin.	Red cells.	Result.
0.025 c.c.	0.1 c.c.	0.5 c.c.	0.5 c.c.	0.5 c.c.	=
0.05 c.c.	...	0.5 c.c.	0.5 c.c.	0.5 c.c.	-
Antigen prepared from patient's own bacteria.					
0.02 c.c.	0.1 c.c.	0.5 c.c.	0.5 c.c.	0.5 c.c.	++
0.01 c.c.	0.1 c.c.	0.5 c.c.	0.5 c.c.	0.5 c.c.	++
0.005 c.c.	0.1 c.c.	0.5 c.c.	0.5 c.c.	0.5 c.c.	+
0.04 c.c.	...	0.5 c.c.	0.5 c.c.	0.5 c.c.	-
...	0.2 c.c.	0.5 c.c.	0.5 c.c.	0.5 c.c.	-
Known typhoid serum.					
Antigen.					
0.025 (stock)	0.1 c.c.	0.5 c.c.	0.5 c.c.	0.5 c.c.	++
0.02 (patient's)	0.1 c.c.	0.5 c.c.	0.5 c.c.	0.5 c.c.	++
Known negative serum.					
0.025 (stock)	0.1 c.c.	0.5 c.c.	0.5 c.c.	0.5 c.c.	-
0.02 (patient's)	0.1 c.c.	0.5 c.c.	0.5 c.c.	0.5 c.c.	-

On reviewing the literature, the author has found that this question of specificity has been worked out experimentally by Raskin.²⁴ Rabbits were immunized against typhoid bacteria, each animal receiving a different strain. While the antibodies of some strains would react with an antigen made from another strain, the opposite also took place; that is, the antibodies produced by one strain would fix complement only with an extract made from that particular strain. The agglutination test was less specific.

On account of this apparent marked difference, the antigen used in the latter part of the author's (Garbat) complement-fixation work was prepared from twenty-seven different typhoid strains isolated from former patients at the hospital. (Even this number of strains could be increased.)

The *technique* of the typhoid complement-fixation reaction is the same as that in the Citron modification of the original Wassermann test, but one-half the quantities are employed:

TECHNIQUE OF THE REACTION.

Antigen.	Serum from X.	Complement.	Hemolysin.	Sheeps' red cells.	Result.
c.c.	c.c.	c.c.	c.c.	c.c.	
(1) 0.025	0.1	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	No hemolysis
(2) 0.0125	0.05	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	No hemolysis
(3)	0.1	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	Hemolysis
Controls. Known typhoid serum.					
(1) 0.025	0.1	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	No hemolysis
(2) 0.0125	0.05	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	No hemolysis
(3)	0.1	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	Hemolysis
Known negative serum.					
(1) 0.025	0.1	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	Hemolysis
(2) 0.0125	0.05	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	Hemolysis
(3)	0.1	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	Hemolysis
(4) 0.5	0.5 (1 to 10)	0.5 (1 to 1000)	0.5 (1 to 20)	Hemolysis

²⁴ Loc. cit.

LIST OF CASES EXAMINED.²⁵

No.	Date.	Stage of disease.	Widal test.	Blood culture.	First complement-fixation test.	Second complement-fixation test.	Third complement-fixation test.	Fourth complement-fixation test.	Remarks.
3	July 23, 1912	First to second week	+	++	4+	Died. Autopsy showed beginning swelling of Peyer's patches.
6	Aug. 2, 1912	"	+	++	2+	
11	Aug. 6, 1912	"	+	++	1+	A very severe, irregular typhoid. Died.
22	Sept. 14, 1912	"	±	++	1+	
24	Sept. 20, 1912	"	+	++	2+	
26	Sept. 20, 1912	"	+	++	4+	
4	Aug. 12, 1912	Second week	±	++	4+	
10	Aug. 10, 1912	"	±	++	4+	Died before repeating test. Typhoid bacteria isolated from spleen. At first diagnosed as miliary tuberculosis. Recovered.
12	Aug. 14, 1912	"	±	++	4+	
13	Aug. 14, 1912	"	±	++	4+	
19	Aug. 28, 1912	"	+	++	3+	
21	Sept. 10, 1912	"	+	++	3+	
25	Sept. 20, 1912	"	+	++	3+	
27	Sept. 20, 1912	"	+	++	3+	
28	Sept. 27, 1912	"	+	++	3+	
29	Sept. 27, 1912	"	±	++	3+	
34	Dec. 6, 1912	"	±	++	3+	
35	Dec. 27, 1912	"	+	++	4+	Died before repeating test. Typhoid bacteria isolated from spleen. At first diagnosed as miliary tuberculosis. Recovered.
36	May 9, 1913	Third week	+	++	4+	
33	Nov. 28, 1912	"	+	++	4+	
23	Sept. 11, 1912	"	+	++	2+	
3	Aug. 2, 1912	"	+	++	4+	
9	Aug. 6, 1912	"	+	++	4+	
14	Aug. 14, 1912	"	+	++	4+	
16	Aug. 28, 1912	"	+	++	4+	
17	Aug. 28, 1912	"	+	++	4+	
18	Aug. 28, 1912	"	+	++	4+	
20	Aug. 28, 1912	"	+	++	4+	Died before repeating test. Typhoid bacteria isolated from spleen. At first diagnosed as miliary tuberculosis. Recovered.
32	Nov. 28, 1912	Fourth week	+	++	3+	
8	Nov. 6, 1912	"	±	++	1+	
37	May 9, 1913	Eighth week	+	++	2+	
30	Sept. 27, 1912	Convalescent	+	++	4+	
31	Sept. 27, 1912	"	+	++	4+	
1	July 23, 1912	"	+	++	4+	
2	July 23, 1912	"	+	++	4+	
7	Aug. 6, 1912	"	+	++	4+	
15	Aug. 21, 1912	"	+	++	2+	

²⁵ Tabulated according to the stage of infection.

The results are reported as 4+, 3+, 2+, 1+, \pm , and —, but no definite diagnosis was made on a 1+ or \pm reaction. A reaction is 4+ when there is no hemolysis in tubes 1 or 2; 3+ when no hemolysis in 1, and slight hemolysis in 2; 2+ when no hemolysis in 1, and complete hemolysis in 2; 1+ when slight hemolysis in 1, and complete hemolysis in 2; \pm when faint turbidity is present in 1; — when complete hemolysis exists in both 1 and 2.

In this manner 37 cases were examined in the various stages of the typhoid infection from the early onset to the late convalescent period. Out of this group, 36 sooner or later gave a strong positive reaction. If negative, the reaction was repeated every five to seven days.

25 were positive on the first examination.

5 became positive on the second examination.

5 became positive on the third examination.

1 became positive on the fourth examination.

1 remained negative. This patient died several days after admission to the hospital, so that the test was not repeated.

How Early in the Infection May the Complement-fixation Bodies Be Detected in the Blood? This answer is difficult, because of the inexactness associated with telling in what stage of the disease the patient is at a particular time. Each clinician has his own method of calculation. In the above table the author estimated this period, by counting back from the onset of abnormal temperature. That the complement-fixation test may be obtained in a very early stage of the disease was proved by Case 3, where the patient died of an extreme toxemia, and at autopsy the Peyer's patches were found just beginning to become swollen; surely not later than the end of the first or early part of the second week. In the majority of instances, however, the reaction appears toward the end of the second or early part of the third week (at a time when the blood culture tends to be negative), and becomes stronger as the disease advances toward convalescence. From the above statistics:

No of cases.	Stage of disease.	Positive results (at the first examination).
18	First and second weeks	8, or 45 per cent.
19	After second week	17, or 90 per cent.

Lüdkke²⁶ too has found that the test appears during the second week. Hirschfeld²⁷ reports a positive reaction as early as the sixth to the eighth day of the infection.

How Long after the Acute Infection Does the Positive Test Persist? A greater number of cases would, of course, enable us to give a more conclusive and definite answer. As a general rule, the reaction is still obtained, and very strongly so too, six to eight weeks after the temperature has become normal. In two patients it was still

²⁶ Loc. cit.

²⁷ Loc. cit.

positive four months afterward. One of these became a typhoid carrier with bacteria in the urine. Three patients who had typhoid fever two years previously, gave a negative reaction, although in one the Widal test was still positive (1 to 50). One patient who had an infection seven years ago and one fifteen years ago were negative. It would be of importance to test this reaction in the blood of typhoid carriers, especially those of long standing. Schöne²⁸ reports three such. One a carrier of ten years' standing, the second of three and one-half years, and the third of three months' duration. In all the fixation was positive. Agglutinins were present only in the third.

Throughout the experiments it seemed that individuals who ran a severe or protracted type of disease developed the complement-fixation bodies less readily or later in the course than the others. While this fact holds true in a great number of instances, it cannot, however, be advocated as a guiding principle of prognosis. Thus Case 3, where the patient had a most severe infection and died several days after admission to the hospital, the complement-fixation test was strongly positive, even though, as was proved by postmortem examination, the patient was at the end of the first or beginning of the second week of the disease.

As to the clinical specificity of the reaction, sera from patients with the following diseases have been tested: La grippe, gastro-duodenitis, trichiniasis, syphilis in the various stages treated and untreated, malaria, tuberculosis, pneumonia, perinephritic abscess, appendicitis, plumbism, and pelvic abscess. Numerous normal sera were also controlled. All gave a negative reaction. Occasionally a doubtful result would be noted, but never a distinct inhibition of hemolysis. One patient with an infective endocarditis, from whose blood the *Streptococcus viridans* was isolated, gave a positive (++) reaction on one examination, but repetition of the test with another specimen of blood taken in several days elicited a negative result. Another patient with a marked mitral endocarditis, no bacteria in the blood and only slight temperature, repeatedly gave a strong positive reaction. A history of several weeks' illness at home with high fever was obtained, but no definite diagnosis of typhoid fever. The possibility of this protracted illness having been typhoid, with the endocarditis as a sequel (there being no other distinct etiological factor) was strongly suspected. In another instance the complement-fixation test proved even more specific than the agglutination test. The serum from a case of *Staphylococcus aureus* sepsis with multiple abscesses of the kidney, gave an agglutination with typhoid bacteria, in dilution 1 to 50, but no complement-fixation test. (At postmortem no evidences of a typhoid infection could be discovered).

In 32 cases sufficient blood was taken at the first examination for the complement-fixation test, the Widal test, and the blood culture, so that comparative studies of the three could be made (see Table). Tabulated according to parallel results obtained, out of 18 cases during the first and second weeks of the disease and 14 cases more advanced there were:

Total number.	First and second weeks.	Later than second week.	Widal test.	Blood culture.	Complement-fixation test.
12	1	11	+	—	+
6	4	2	+	+	+
5	5	—	+	+	—
3	3	—	—	+	+
2	2	—	—	+	—
2	2	—	—	—	+
1	1	—	+	—	—
1	1	—	—	—	—

It is observed that there is no absolute uniformity in these findings. All possible combinations may occur, especially in the early stages of the disease. In the later stages, however, the general rule was a positive Widal and complement-fixation test and a negative blood culture.

If one considers the frequency with which each test by itself was positive, the following is noted:

Widal	+ in 24 cases (11 out of 18 in first two weeks, 13 out of 14 later on)
Blood culture	+ in 16 cases (14 out of 18 in first two weeks, 2 out of 14 later on)
Complement-fixation	+ in 23 cases (10 out of 18 in first two weeks, 13 out of 14 later on)

Thus complement fixation was present as frequently as the positive Widal test, and was then of great corroborative value. In two cases (12 and 13) it was positive even before the Widal or the blood culture. Similar experiences are reported by Spät²⁹ and Hirschfeld.³⁰ That the blood culture was positive in only 50 per cent. of our cases is probably accounted for by the better class of our ward patients. They are treated at home for a longer period of time, and thus come to the hospital when there is less likelihood of still finding the bacteria in the blood.

In conclusion the following summary may be given:

1. Practically all typhoid fever patients examined, sooner or later developed antibodies in their serum, which were demonstrable by the method of complement-fixation. These bodies increase in number with the progress of the disease and are especially numerous during convalescence.

2. A highly polyvalent antigen properly prepared is absolutely essential in order to obtain a maximum of positive results.

3. Strains of typhoid bacteria may differ from each other in that their respective antibodies cannot fix complement with an antigen made from a different strain.³¹

²⁹ Loc. cit.

³⁰ Loc. cit.

³¹ With this experience in mind, the author has always employed a polyvalent typhoid vaccine for prophylactic antityphoid inoculations.

4. There is no definite relationship between the occurrence of a positive Widal and complement fixation test on one hand with a positive blood culture on the other.

5. When the blood culture is negative, as so frequently happens in the later stages of typhoid fever, a positive complement-fixation test throws great corroborative diagnostic weight on the side of a doubtful or positive Widal reaction. Occasionally the test is positive before the Widal or blood culture.

6. The very simple technique for obtaining 1 c.c. of blood from the patient's ear or finger when the veins are not suitable, stands out prominently in contrast to the extensive, and at times impossible preparations required for a blood culture. The ease of transportation of the specimen of blood must also be considered.

The writer must thank the medical attendings of the hospital for granting him the privilege of these examinations. Without their kind and constant coöperation this work would have been impossible.

RELATION OF LESIONS OF THE SMALL INTESTINE TO DISORDERS OF THE STOMACH AND CAP AS OBSERVED ROENTGENOLOGICALLY.

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THE relation of lesions of the small intestine to disorders of the stomach has been recognized for many years by clinicians, most notably perhaps in the vomiting, pain, and tenderness referred to the right hypochondrium in cases of appendicitis, and in the gastric symptoms manifested by acute intestinal obstruction. Mayo has compared the stomach to a fire-alarm box, and has called attention to the futility of trying to extinguish the fire by squirting water on the alarm box. In a recent article read before the American Roentgen Ray Association,¹ Crane quoted Mayo's simile, and cited instances in which he also had observed gastro-intestinal symptoms with roentgenological evidence of a lesion at some distant point. In this communication I shall try to show that the roentgenologist can detect the first sign of smoke, and after searching farther, can usually find the location of the fire itself.

TERMINOLOGY. Before entering upon any discussion an explanatory word should be said concerning terminology. While the roentgenological findings of the gastro-intestinal tract differ in every individual, I have come to recognize certain findings as

¹ Boston, October, 1913.

usual and others as unusual. In this communication the term *usual* will be applied to those findings which are most common, that is to say, normal, so far as I have been able to determine, and the term *unusual* will be applied to uncommon roentgenographic findings, which are associated with symptoms.

THESIS. As a working basis it will be necessary to describe the physiology of the duodenum, jejunum, and ileum as observed roentgenologically, and to compare the unusual findings with the usual findings. It will be seen that certain phenomena in the small intestine are frequently accompanied by peculiar manifestations in the stomach and cap. These gastric manifestations, viz., primary and secondary evidences of spasm and their opposites, atony or lack of peristalsis of the pylorus, pyloric sphincter and cap, must next be described. Upon this foundation we shall build up the superstructure which is the main subject of this communication—that iliac stasis, and particularly iliac dilatation, are directly related to and responsible for certain spasms and even organic lesions of the pylorus, pyloric sphincter, and cap. In conclusion, we shall estimate the value of the roentgenological evidence for determining in each individual case whether or not surgical procedure is indicated, or what other method of treatment is advisable.

TECHNIQUE. In order to obtain the findings upon which our observations are based, an extensive routine examination of the entire gastro-intestinal tract is essential. Although the technique employed is being elaborated continually, a brief description of the present method may be of interest.

About 11 P.M., or ten hours before the roentgenographical examination, the patient takes bismuth or barium suspended in buttermilk, in conjunction with a meal of meat, potatoes, and bread. At 9 o'clock the next morning he presents himself for examination. A roentgenogram of the whole abdomen is made to determine how far the meal taken the night before has progressed. This information can usually be obtained from the fluoroscopic examination, which is made simultaneously; but if any doubt exists the plate should be developed rapidly in order to ascertain with certainty whether or not the ileum is empty. If food still remains in the ileum the same examination is repeated bi-hourly until the ileum is completely evacuated, then the patient takes bismuth or barium suspended in buttermilk. After the passage of the ingesta through the esophagus has been observed fluoroscopically the stomach is examined by combined fluoroscopy and serial roentgenography.

SERIAL ROENTGENOGRAPHY OF THE STOMACH. Twelve roentgenograms are made in the prone posture, four to six in the lateral direction, two posteriorly, and twelve with the patient erect, after which the patient at once eats a meal of meat, potatoes, and bread. Two hours later another series of six to twelve roentgeno-

grams is made, two of them stereoscopic roentgenograms of the entire gastro-intestinal tract. As this series often gives the most valuable information, we are therefore increasing the number of exposures made at this time. If further details concerning the progress of gastric digestion seem desirable, another series of roentgenograms is made four hours after ingestion. A pair of stereoroentgenograms is invariably taken six hours after the bismuth meal. If at this time the fluoroscope reveals an appreciable gastric retention, five or six roentgenograms of the stomach are made.

EXAMINATION OF ILEOCECAL REGION.—As the condition of filling in the ileocecal region is of prime diagnostic importance at this time, two small stereoroentgenograms (8 x 10 inches) are made of this portion of the tract, and if marked stasis or any other unusual finding is observed fluoroscopically, six to eight small roentgenograms of this region are made. Two hours later, *i. e.*, eight hours after ingestion, one plain roentgenogram or a pair of stereoroentgenograms is made. This completes the examination for that day. At nine o'clock the next morning, *i. e.*, twenty-four hours after the ingestion of bismuth and buttermilk, another roentgenogram is obtained. If there is evidence of colonic stasis or constipation a roentgenogram is made every twenty-four hours until the colon is evacuated. In case the patient habitually depends upon a cathartic, it should be allowed as usual, but an active purgative is undesirable.

After the examination just described there remains to be made an examination of the gall-bladder for possible calculi, and also an examination of the colon, while mechanically distended, for the purpose of discovering any spasmodic or organic lesions not detected when the bismuth passed through from above.

The night before this examination an active cathartic is administered. If this is not effective the patient takes a saline cathartic early in the morning, but on no account an enema, as this might be retained and dilute the bismuth clyster, which is used to distend the colon.

EXAMINATION OF GALL-BLADDER. Before the colon is examined, roentgenograms are made over the gall-bladder region, as biliary calculi can be detected in at least 50 per cent. of the cases when they are present.²

EXAMINATION OF THE COLON. A clyster of bismuth or barium, mucilage of acacia, and hot water (barium sulphate 3v, mucilage

² Case, The X-ray Examination of the Liver and Gall-bladder, Arch. of Roent. Ray., September, 1913; Roentgenoscopy of the Liver and Biliary Passages, with Special Reference to Gall-stones, Jour. Amer. Med. Assoc., September 20, 1913. Cole, Roentgenographic Diagnosis of Gall-stones and Cholecystitis, Surg., Gyn., and Obst., February, 1914, vol. xviii, No. 2. Pfahler, Die Roentgenstrahlen als Hilfsmittel bei der Gallensteindiagnose, Fort. a. d. Geb. d. Roent., April, 1911. N.H., xvi, B. 5, pp. 335-337. Gastric and Duodenal Adhesions in the Gall-bladder Region and Their Diagnosis by the Roentgen Ray, Jour. Amer. Med. Assoc., June 17, 1911, vol. lvi, No. 24, pp. 1777-1779.

of acacia ℥xij, hot water q. s., ℥xxx) is now administered and retained by the patient while a pair of stereoroentgenograms of the colon are made. It is a wise procedure to make a third plain roentgenogram or another pair of stereoroentgenograms, because it is sometimes difficult to differentiate between spasms and organic lesions in a single pair of stereoroentgenograms.

The gastro-intestinal tract has now been completely examined by successive series of roentgenograms made immediately after the bismuth meal, and at intervals thereafter of two hours, four hours, six hours, eight hours, ten hours, twelve and fourteen hours twenty-four hours (if necessary), forty-eight hours, and seventy-two hours, and by one or more pairs of stereoroentgenograms of the colon, made after a bismuth clyster has been administered.

Such a series of roentgenograms, viewed upon a light box, where they may be studied individually and collectively, gives a wealth of information. By carefully studying the findings in one region and comparing them with the findings in other portions of the tract it is often possible to unravel the most complicated cases.

VALUE OF COMPLETE GASTRO-INTESTINAL EXAMINATION. A study of about 300 such cases, showing the stomach, small intestine, and colon at various intervals after the ingestion of food, has revealed a great variety of significant findings, a correlation of which leads me to the publication of this preliminary report.

ERRONEOUS METHODS OF DETERMINING GASTRO-INTESTINAL MOTOR EFFICIENCY. Many of the previous roentgenological observations on iliac stasis have been unreliable, because the bismuth has been mixed with or suspended in unsuitable mediums, and because the period required for iliac evacuation has been reckoned from the time when the bismuth was administered, instead of being reckoned from the time when the last trace of it left the stomach. Other conditions, such as recent catharsis, which so often precedes a gastro-intestinal examination, undoubtedly affect the motor phenomena.

In a previous communication³ I have already shown the fallacy of testing the gastric motor efficiency by administering bismuth suspended in fluid or mixed with cereal, and the same is true for intestinal motor efficiency. If the test is to be of value the stomach and intestines must be called upon to evacuate such a meal as is normally imposed upon them. Therefore the true test of gastro-intestinal motor efficiency is made by administering bismuth or barium, suspended in fluid, preferably buttermilk, *in conjunction with* a Riegel meal of meat, potatoes, and bread.

An even more fertile source of error is dating the period of iliac retention from the time of ingestion. For instance, if the stomach

³ Die Diagnose der Boesartigen und Gutartigen Magen—und Duodenal-Laesionen und ihre Unterscheidung durch Serien-Roentgen-Aufnahmen, Zeitschrift f. klinische Medicin, Berlin, 1914, 79, B. H., 5 u. 6.

is high and of the cow-horn type, especially if a condition of diminished acidity or achylia exists, evacuation will be accomplished very rapidly, perhaps in two hours, whereas many a stomach, presenting no organic obstruction, requires six hours for complete evacuation. Suppose now that in both cases the ileum is just evacuated ten hours after ingestion. According to the old method of reckoning, both cases present the same degree of iliac stasis, although, as a matter of fact, one case presents an eight-hour while the other presents only a four-hour iliac retention. The time required for bismuth impregnated food to pass through the small intestine may be corroborated by reckoning the speed with which the next succeeding meal, not impregnated with bismuth, displaces that previously ingested, or mixes with it at the cecum.

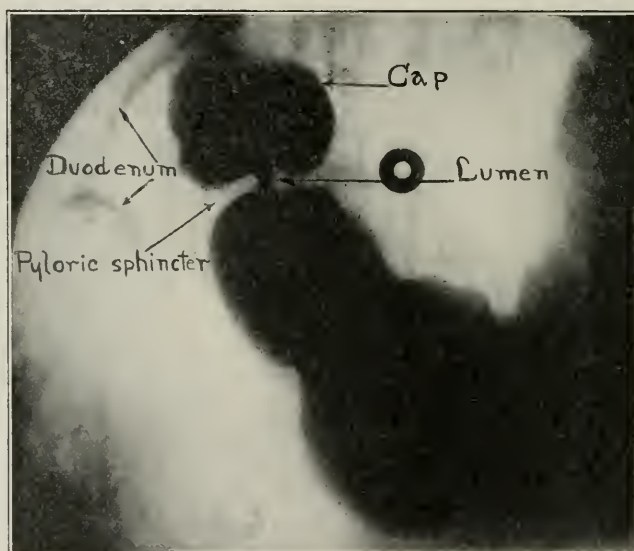


FIG. 1.—Normal cap (pilleus ventriculi).

KNOWLEDGE OF ROENTGENOLOGY OF THE STOMACH AND CAP AN ESSENTIAL TO AN UNDERSTANDING OF THIS COMMUNICATION. In previous communications, which are, in a way, introductory chapters to the present work. The physiological characteristics and motor phenomena of the pyloric sphincter and pilleus ventriculi (cap)⁴ as observed roentgenographically has been described. In fact this information constitutes the *sine qua non* of roentgenological diagnosis of the gastro-intestinal tract. It has been shown

⁴ Arch. of Roent. Ray, December, 1911, p. 242; Amer. Quart. of Roent., March, 1912, vol. iii, No. 4, p. 1. Arch of Roent. Ray, October, 1912, No. 147, p. 172; Jour. Amer. Med. Assoc., November 30, 1912, vol. lix, p. 1947.

that the region previously termed the first or ascending portion of the duodenum is not the duodenum in any sense, but is actually the cap of the stomach (*pilleus ventriculi*) (Fig. 1). Its anatomy and physiology as observed roentgenologically and the lesions to which it is subject have been described.⁵ Therefore in this communication we may begin with the descending portion of the duodenum.

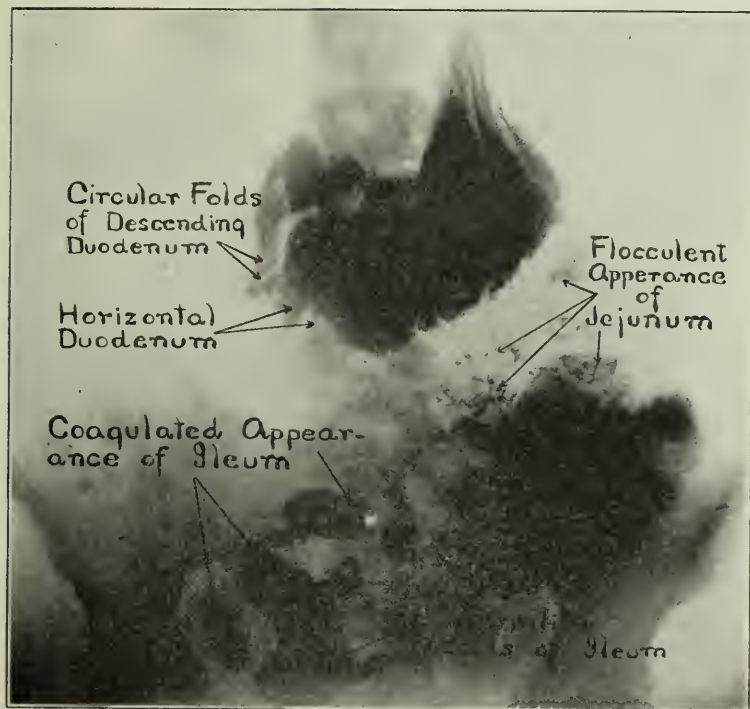


FIG. 2.—Usual roentgenographical appearance of cap, duodenum, jejunum, and ileum.

USUAL FINDINGS IN THE DUODENUM. Embryologically the descending and not the ascending duodenum is the proximal end of the midgut. Anatomically it exhibits small, irregular, circular folds, particularly on its posterior aspect. It descends at an acute angle from the top of the cap, and in conjunction with the horizontal portion, fits around the head of the pancreas, occupying a fixed position. As it frequently passes down behind the stomach it may be obscured by the pars pylorica, except where it extends above and below the stomach. It can be identified by its shape, and position and the ring-like appearance of its circular contractions (Figs. 1, 2, and 3). Its motor phenomena is a broad, rapid,

⁵ Arch. of Roent. Ray, April, 1912, No. 141, p. 425; Jour. Amer. Med. Assoc., September 6, 1913, vol. lxi, No. 10, p. 762.

periodical, propulsive peristalsis, and a churning or mixing motion of the circular folds.

USUAL FINDINGS OF THE JEJUNUM. From the horizontal duodenum the ingesta pass into the jejunum in the upper left quadrant of the abdomen, where they are broken up into finely comminuted particles. Roentgenographically these fragments present the flocculent appearance which distinguishes the jejunum from the rest of the small intestine (Figs. 2 and 3).



FIG. 3.—Withdrawal of chyme from cap by broad propulsive peristalsis of duodenum.

USUAL FINDINGS OF THE ILEUM. As the chyme reaches the centre of the small intestine and occupies the ileum it begins to form into coagulated masses. Upon reaching the terminal portion of the ileum these coagulated masses collect in long, worm-like coils, and as they near the cecum they fill the lumen of the gut, so that frequently one can identify several continuous convolutions of the ileum, especially if the roentgenograms are studied stereoscopically. The ileum, therefore, is recognized roentgenographically by its location in the right lower quadrant of the abdomen and the coagulated appearance of the contents in its upper portion (Fig. 2),

and the well-defined worm-like coils in its lower portion (Figs. 2, 10, 15, and 16).

PHYSIOLOGY OF THE SMALL INTESTINE AS OBSERVED ROENTGENOGRAPHICALLY. The characteristic roentgenographic findings by which the various portions of the small intestine may be thus identified are the result of certain physiological phenomena, expressed roentgenologically in terms of motor activity.

MOTOR PHENOMENA OF THE DUODENUM. The descending duodenum obtains the ingesta by means of broad peristaltic contractions (Fig. 3), which withdraw the chyme from the reservoir cap, where it collects after being expelled through the pyloric sphincter during the systole of each gastric cycle. Duodenal peristalsis occurs periodically, but not coincidentally with or at the same rate, as gastric peristalsis. The chyme is thus propelled through the duodenum in the finger-like masses described by Holzkecht (Fig. 3). During the early stage of digestion this process takes place very rapidly, because the contents of the cap are only slightly acid and mostly fluid, having been expelled through a more or less tightly contracted sphincter.

MOTOR PHENOMENA OF THE JEJUNUM. Roentgenographic observations have proved that the name jejunum was well chosen by the ancients from their postmortem investigations, for the peristalsis of this portion of the tract is so rapid that the jejunal lumen is seldom seen dilated or even filled.

MOTOR PHENOMENA OF THE ILEUM. The ileum retains the food longer than any other portion of the small intestine. It lodges here temporarily, after being passed rapidly through the cap, duodenum, and jejunum.

ROENTGENOLOGIC APPEARANCE OF SMALL INTESTINE PARTLY DUE TO CONSISTENCY OF CONTENTS. The flocculent appearance of the jejunum, coagulated appearance of the upper ileum, and worm-like coils of the lower ileum are probably caused, in part at least, by the consistency of the contents as well as by the peristalsis characteristic of each region. When a clyster passes back through an incomplete ileocecal valve, filling the ileum and even distending the jejunum, the roentgenological findings peculiar to different portions of the small intestine do not present.

UNUSUAL FINDINGS OBSERVED IN THE SMALL INTESTINE ILLUMINATE MANY OBSCURE FUNCTIONAL GASTRO-INTESTINAL LESIONS. Variations from the above-described motor phenomena of the small intestine cause unusual roentgenographical findings, which illuminate, I believe, many of the obscure functional and even organic disorders of the gastro-intestinal tract. A description of all of the roentgenological findings associated with functional gastric derangements would form an extensive communication in itself. In this paper we can only enumerate and briefly describe those usually associated with lesions of the ileocecal region. Such

functional gastric disorders present the following roentgenological findings:

- | | | |
|---|---|----------------------------|
| 1. Spasms of | { | (a) the pars pylorica. |
| | | (b) the pyloric sphincter. |
| | | (c) the cap. |
| 2. Results of spasms, indicated by permanent changes in | { | (a) the pars pylorica. |
| | | (b) the pyloric sphincter. |
| | | (c) the cap. |
| 3. Gastric retention without pylorospasm. | | |

SPASMS OF THE PARS PYLORICA, PYLORIC SPHINCTER, AND CAP.
There are two ways of ascertaining that the pars pylorica, pyloric sphincter, or cap is subject to spasmodic contraction. The spasm itself may be registered on some or all of the roentgenograms of the series in the very act of occluding the lumen. Or only the results of the spasm may be visible in a permanent diminution of the lumen, caused by constant or spasmodic contraction of the muscular coat.

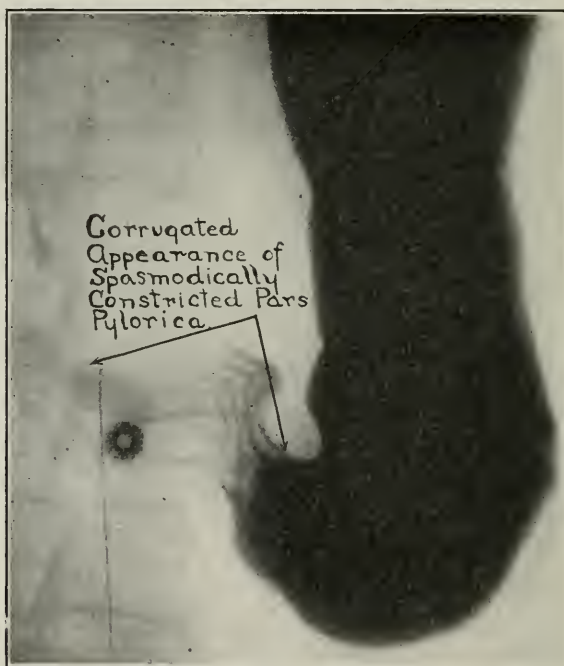


Fig. 4, a.—Spasmodic constriction of pars pylorica.

SPASM OF THE PARS PYLORICA. The roentgenographical picture of spasmodic contraction of the pars pylorica shows that portion of the gastric lumen reduced in size out of all proportion to the dimensions of the pars media and pars cardiaca. The whole or only the pyloric end of the region may be distorted. The mucosa and

submucosa, normally ribbed by shallow rugæ, are puckered into deep folds, which give the lumen a corrugated appearance (Fig. 4, *a*). These furrows may run transversely or obliquely. The roentgenogram which presents these phenomena may be followed by one showing a perfectly smooth, well-distended contour of the same region, indicating that the spasm has relaxed its grip temporarily (Fig. 4, *b*). Sometimes the spasm occurs only at a certain stage of digestion, and is absent in all the roentgenograms made before and after this interval.

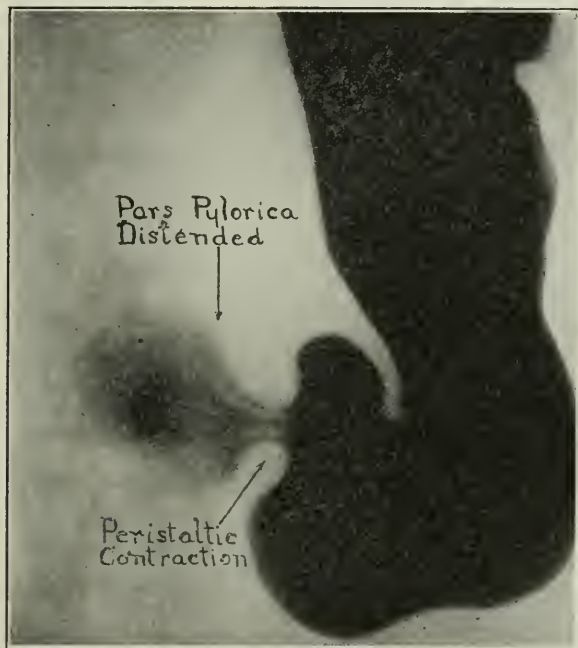


FIG. 4, *b*.—Relaxation of spasm illustrated in Fig. 4, *a*.

SPASM OF THE PYLORIC SPHINCTER. The presence of a spasmodic constriction of the pyloric sphincter may be inferred from the absence of bismuth in the lumen of the sphincter and cap, provided the bismuth is seen passing freely from the stomach into the cap in roentgenograms made previously and subsequently (Fig. 5, *a* and 5, *b*). If the cap is quickly evacuated by duodenal peristalsis, its outlines will remain indistinct or invisible until a relaxation of the pyloric sphincter opens the passage from the pars pylorica through which the cap is resupplied with contents:

In spite of Kreuzfuch's reports to the contrary, my observations have been that the gastric peristalsis may be just as active while a spasm involves the pyloric sphincter as it is when the sphincter is functioning normally.

SPASM OF THE CAP. Constriction of the cap from spasmodic contraction presents roentgenographical evidence similar to that

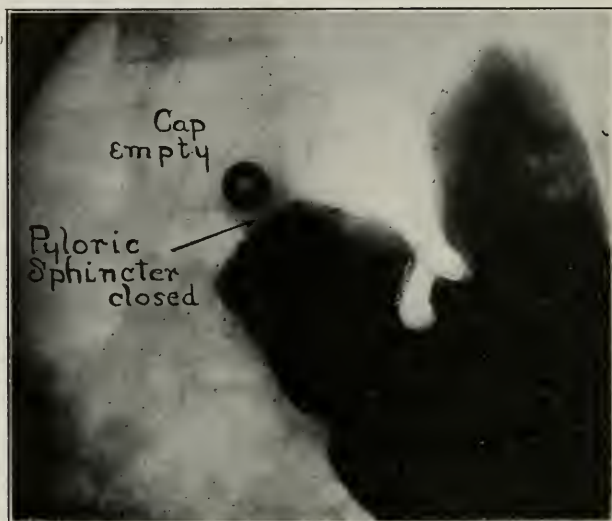


FIG. 5, a.—Spasmodic constriction of pyloric sphincter.



FIG. 5, b.—Relaxation of spasm illustrated in Fig. 5, a.

caused by a spasm of the colon. The cap has the appearance of having been twisted or wrung empty of its contents, only a sugges-

tion of its bismuth impregnated contents being visible, caught or entangled under the constricting folds. As a result the distorted lumen casts a corrugated or fluted shadow on the roentgenograms (Fig. 6). An interesting case of this kind, presenting definite symptoms of ulcer of the cap, was referred to me from a hospital for the sake of increasing the number of my postpyloric ulcer cases. The clinical history was so typical that I economized by making only about half the usual number of roentgenograms. Even this limited series proved enough to justify a negative diagnosis of chronic indurated duodenal ulcer, that is, an ulcer indicating surgical procedure. Most of the roentgenograms showed definite graphic evidence of a spasm of the cap. In two instances, however,



FIG. 6.—Spasmodic constriction of cap, caused by chronic appendicitis. Proved by operation.

a fully distended well-defined cap presented a perfectly normal picture. I therefore reported that the lesion was spasmodic rather than organic, although the spasm might possibly be caused by a superficial postpyloric ulcer. This negative report delayed operation for the duodenal ulcer, which had been diagnosed by other means. Two days later the patient's symptoms culminated in a definite attack of acute appendicitis, for which an emergency operation was performed. The clinical diagnosis of duodenal ulcer had been made so positively, and the history had been so definite that I permitted myself to dispense with a complete gastrointestinal examination, and allowed a preconceived theory to distract my mind from considering a lesion of the right iliac fossa

as the origin of the spasm, although in several previous cases I had recognized a similar interrelation. The moral of this is, "Don't let a perfectly typical history of some condition deter you from making a complete examination."

PERMANENT CHANGES IN THE PARS PYLORICA, PYLORIC SPHINCTER, AND CAP. All of the findings described thus far have been direct evidence of the spasm itself. Let us now consider the roentgenological findings of those permanent changes which result from long-continued spasms of the pars pylorica, pyloric sphincter, and cap.

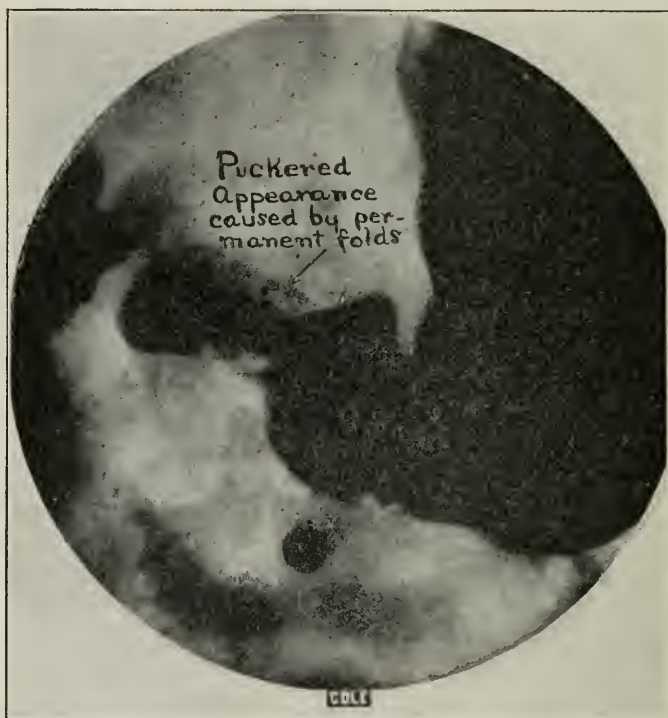


FIG. 7.—Permanent changes in gastric wall, resulting from long-continued spasm of pars pylorica. Proved by operation.

Frequent spasm of the pars pylorica causes a contraction of the muscular coat, and a consequent diminution of the lumen of this region as compared with lumen of the pars media and pars cardiaca. The mucosa and submucosa heap up into deep folds and attain a permanently puckered appearance, such as they formerly presented only when dominated by a spasm. The region lacks pliability, presenting unusually broad peristaltic contractions, but exhibits a regular systole and diastole (Fig. 7).

The result of spasm of the pyloric sphincter is not quite so characteristic. It may be described as a puckering resembling the folds near a purse string that had been tightly drawn, and is most prominent during the stage of diastole, when the adjacent tissue is completely relaxed (Fig. 8). The sphincter may be thicker than normal, but at some stage of digestion its lumen should be distinctly shown.

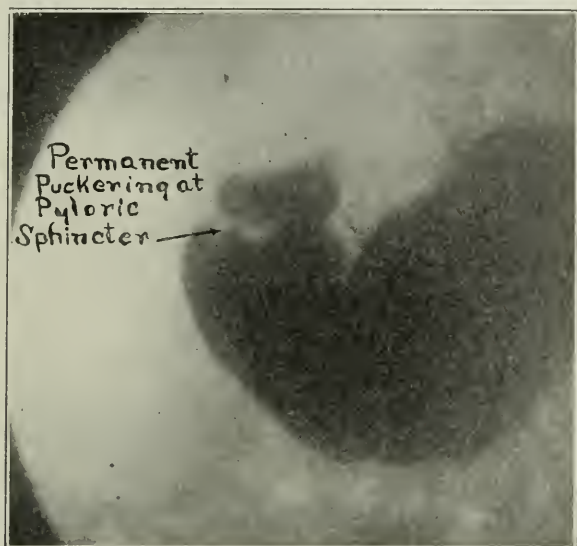


FIG. 8.—Permanent changes in pyloric sphincter, caused by constant spasmodic constriction, a reflex from chronic appendicitis. Proved by operation.

The roentgenological findings of permanent changes resulting from spasm of the cap are so similar to those of postpyloric ulcer that the two conditions are sometimes difficult to differentiate. Such a case is illustrated in Fig. 9. Roentgenographically the cap had the appearance of being cicatricially contracted by an ulcerative process, and the lesion was diagnosed as postpyloric ulcer. Operation revealed chronic appendicitis and redness and swelling of the cap near the pylorus without any evidence of ulceration, obviously the result of constant reflex spasmodic contraction from the diseased appendix.

GASTRIC RETENTION WITHOUT PYLOROSPASM. Having discussed overactivity of the muscularis as a functional lesion of the pars pylorica, pyloric sphincter and cap, let us now consider lack of activity of these same muscular tissues.

Although lack of tonicity is undoubtedly a functional disorder of the stomach, and as such is related to our subject, yet it is not

caused by a lesion at some distant point, so far as we know, and should therefore be omitted here.



FIG. 9.—Permanent changes in cap, resulting from long-continued spasm, a reflex from chronic appendicitis. Resembles the roentgenographical appearance of cicatricial contraction from postpyloric ulcer.

RETENTION IN STOMACH AND CAP DUE TO INHIBITION OF DUODENAL PERISTALSIS. Retention in the stomach and cap longer than the normal time required for digestion is a roentgenological finding of the utmost significance. As digestion progresses there often ensues a diminution or complete inhibition of propulsive duodenal peristalsis and evacuation of the cap is suspended temporarily (Fig. 10). At the same time gastric peristalsis may still continue and even increase its propulsive power, owing to the diminished bulk which it is gripping. Thus the cap, being rapidly filled from the stomach and not evacuated by the duodenal peristalsis, distends during the later stages of digestion to fuller proportions than before (Fig. 10). Sometimes the force of gastric peristalsis is sufficient to expel the chyme through the cap into the descending and horizontal duodenum, but so long as the jejunum remains empty, it is obvious that duodenojejunal peristalsis has stopped functioning. It is the absence of this agent for sucking the food from the cap and propelling it through the duodenum, which explains the gastric and cap retention in many instances, for it cannot be contended that there is any organic or functional disturbance of the stomach or cap, since the chyme courses through

them freely, nor is it tenable to suppose that any organic obstruction exists in the duodenum or jejunum, as the chyme rapidly traversed this region at an earlier stage of digestion.

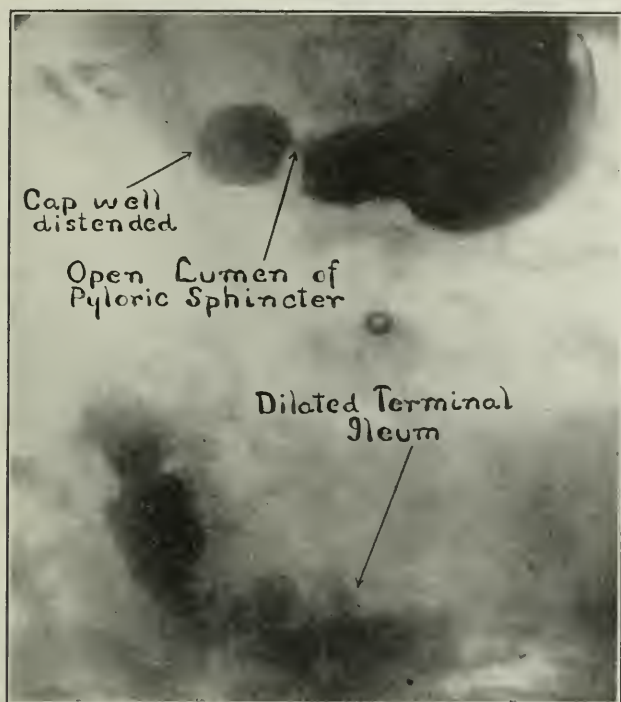


FIG. 10.—Dilatation of terminal ileum, causing inhibition of duodenal peristalsis and resultant gastric and cap retention.

DANGERS OF PROLONGED RETENTION IN THE CAP. Retention in the cap is often the harbinger of organic lesions of the right hypochondrium. It may cause conditions favorable for the production of postpyloric ulcer. As has been stated in previous communications the cap has the function of a reservoir or second stomach, where it is probable that the finishing touches of proteid digestion are applied to the small amount of chyme thus isolated from the bulk of food in the stomach. That the strength of the gastric juices is intensified in the cap may be inferred from the presence here of the glands of Brunner and Lieberkuhn. If duodenal peristalsis ceases after most of the chyme has been withdrawn from the stomach, and an appreciable amount of chyme remains in the cap for a much longer period of time than usual (Fig. 11), is it not reasonable to suppose that this chyme becomes hyperacid from oversaturation with the juices of the secretory glands of the cap? For if it is imprisoned in the cap without being diluted by

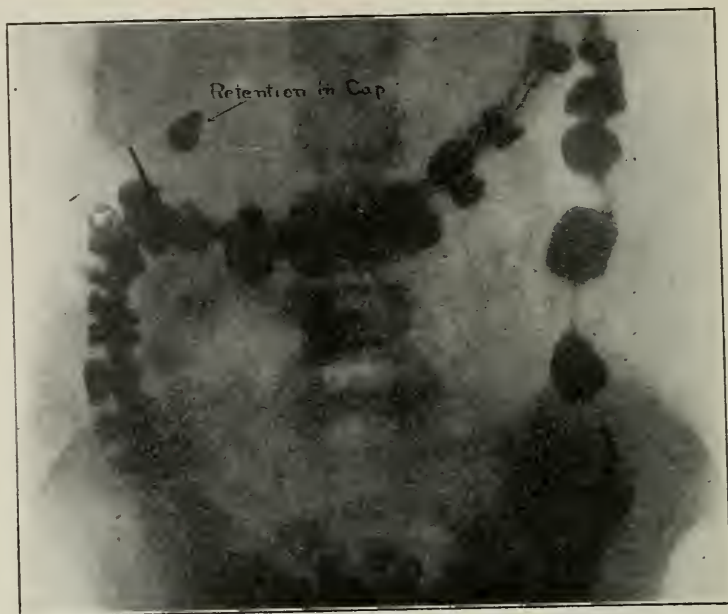


FIG. 11.—Prolonged retention in cap after evacuation of stomach, duodenum, and jejunum.

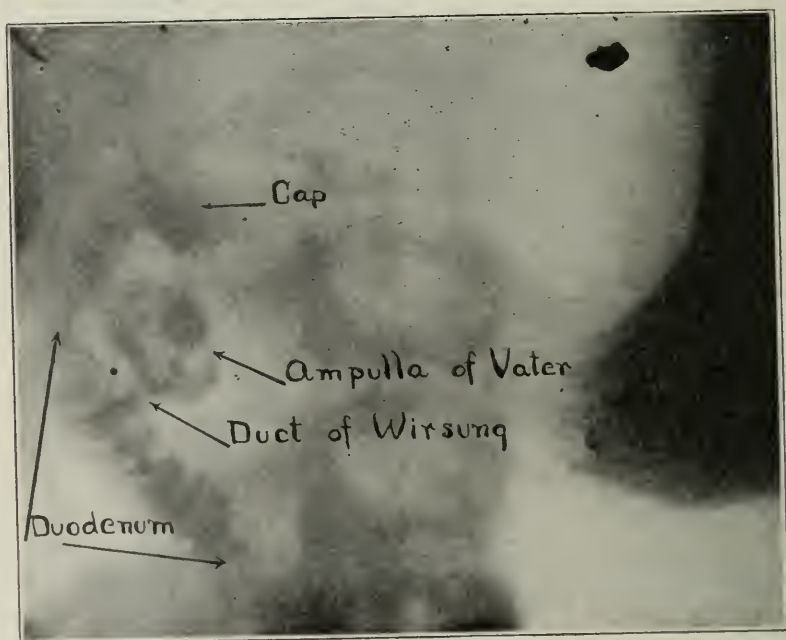


FIG. 12.—Distention of duct of Wirsung and ampulla of Vater by bismuth ingesta.

weaker chyme from the stomach or neutralized by alkaline solutions administered for this purpose an excess of acid must result. Is it not likely, therefore, that a prolongation of this condition will destroy the muscular coat, particularly if the mucosa has been bruised or broken by solid particles of food or by instrumentation? If this supposition be correct, any condition which diminishes, paralyzes, or inhibits duodenojejunal peristalsis will be a predisposing cause of postpyloric ulcer.

It is also important to note the far-reaching results of dilatation of the descending and horizontal duodenum, which may be filled by an active gastric peristalsis and not evacuated for a long time in consequence of the inhibition of duodenal peristalsis. The over-distended lumen offers no resistance to the expulsion of chyme through the duct of Wirsung into the ampulla of Vater (Fig. 12), and perhaps even into the common or cystic duct. This indicates a direct source of gall-bladder infection.⁶

ILIAC DILATATION A CAUSE OF INHIBITION OF DUODENAL PERISTALSIS. Iliac stasis has been the all-absorbing problem of late among clinicians and surgeons interested in gastro-intestinal lesions. Although roentgenological evidence has played an important role in the diagnosis of this condition, interpretation of the findings has been influenced in many instances by the preconceived theory which the surgeon or practitioner was trying to prove. Case's roentgenological studies of the ileocecal region are an exception to this rather general rule.⁷

Careful observation of the entire gastro-intestinal tract at different periods after ingestion has shown that the inhibition of duodenal peristalsis during the later stages of digestion is usually associated with a distention or dilatation of the terminal portion of the ileum. It has been noted that as the chyme accumulates in and distends the ileum, duodenal peristalsis diminishes. The replete ileum, no longer a hungry gut, apparently exerts its influence to prevent overfilling by cutting off the supply from above. The connecting link between the gastroduodenal and ileocecal regions may be a chemical reflex. I suspect that when the ileum becomes replete it curtails through a reflex the amount of bile and pancreatic secretions, so that the alkalinity of the duodenal juices is not sufficiently strong to neutralize the acid or hyperacid chyme expelled from the stomach and rendered more acid by the secretions of the cap. Hence there ensues a cessation of the alternating alkaline and acid reactions of the descending duodenum, the exciting cause for the propulsive duodenal peristalsis, which normally evacuates

⁶ A like duodenal dilatation may also be caused by an organic obstruction at the duodenojejunal junction, by pressure from the mesentery vessels, or by adhesions.

⁷ Case, X-ray Observations on Colonic Peristalsis and Antiperistalsis, with Special Reference to the Function of the Ileocolic Valve, Read before International Congress, London, August, 1913; X-ray Studies of the Ileocecal Region and the Appendix, Amer. Quart. of Roent., November, 1912, p. 77.

the cap and propels the food through the duodenum and jejunum.⁸ This theory presupposes some such chemical influence as the reflex described by Cannon, Marbeau, and Mehring, except that it controls the propulsive duodenal peristalsis instead of the pyloric sphincter. I have observed time and time again that if, after the contents of the stomach and cap have remained stationery for some time, the ileum be partly evacuated a rehabilitation of duodenal peristalsis will be established forthwith and food may be seen leaving the cap and passing forward through the jejunum.

When gastric achylia exists it may be that this reflex is materially altered, as the chyme is neutral or only slightly acid, and can be rendered alkaline by the duodenal secretions with great rapidity. This would account for the rapid evacuation of the stomach in some cases of gastric cancer.

Having demonstrated that gastroduodenal retention may be caused by the inhibition of duodenal peristalsis, and having associated this inhibition with a surfeited ileum, one next seeks to discover why the ileum does not rid itself of an oversupply by passing it forward into the cecum.

Röntgenological evidence indicates that iliac stasis or rather iliac dilatation may be caused by

1. Incomplete evacuation or fecal impaction in the cecum and ascending colon.
2. Various types of membranes and veils involving the colon and terminal cecum.
3. Kinks of the terminal portion of the ileum.
4. Insufficiency of the ileocecal valve.
5. Chronic appendicitis (primary or secondarily from adhesions, either before or after its removal).

All of these conditions may be recognized and differentiated from each other with a remarkable degree of accuracy by a thorough roentgenological examination, preferably in conjunction with a serial roentgenographical examination of the stomach and duodenum.

The symptoms of iliac stasis are rather varied because sometimes the symptoms of the cause prevail, and sometimes the symptoms of the effect prevail, particularly those referable to the stomach and cap. These symptoms will be considered under the discussion of each cause.

COLONIC STASIS. Colonic stasis is perhaps the most common cause of iliac stasis. Since the time when man dispensed with forefeet and assumed the erect posture it has been up-hill work for the ascending colon to evacuate itself. Overdistention of the cecum and ascending colon constitutes a large proportion of colonic

⁸ If I have delved further into the causes of these roentgenological findings than my experience as a physiologist will justify, perhaps my suppositions may stimulate some physiologist to prove or disprove these theories.

stasis. The dilatation and atony of this region is partly compensated for by the active peristalsis of the terminal portion of the ileum. In proof of this, bismuth impregnated feces will be observed in the cecum much longer after a bismuth meal followed by a period of fasting than after a bismuth meal followed by the ingestion of food or possibly water. If the stasis (or constipation) in the ascending colon is persistent, unusual energy is demanded from the peristalsis of the terminal ileum. When its strength is not sufficient to break the blockade, delayed evacuation results, accompanied by a chain of symptoms, perhaps referable directly

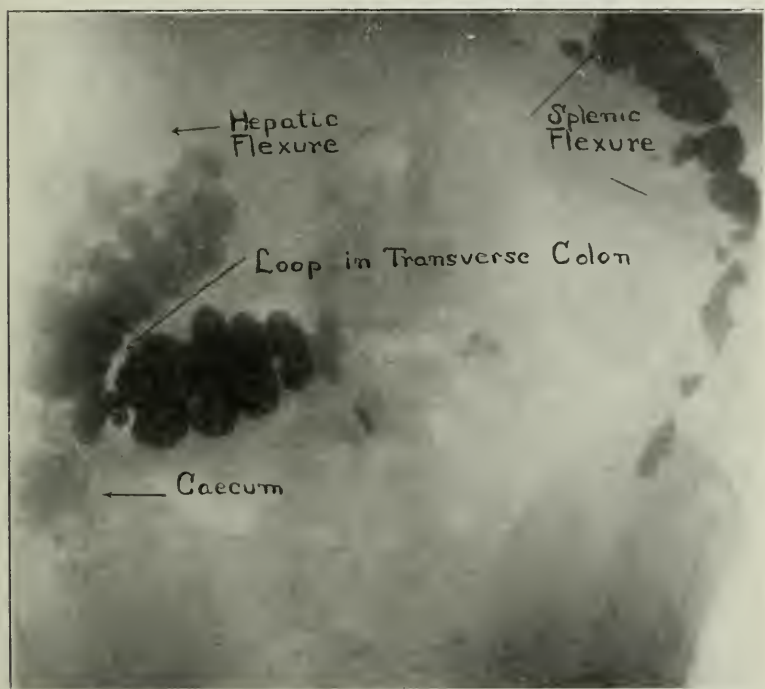


FIG. 13.—Stasis in cecum seventy-eight hours after ingestion.

to the exciting cause, "cecal constipation," or perhaps referred to the stomach and cap, as suggested earlier in this article. To overcome this obstruction, bismuth impregnated chyme may be seen frequently, forcing its way up through the fecal accumulations in the cecum and ascending colon, or the next meal succeeding the bismuth meal may be observed working up through the ascending colon (Fig. 13). If in such cases the cecum and ascending colon can be evacuated by properly applied manipulation, massage or even catharsis, previous to the ingestion of more food, stasis of food in the terminal ileum will thus be diminished, and often

the gastric or duodenal symptoms referred to the right hypochondrium will be relieved. Moreover, lesions in this region of a much more serious character may perhaps be prevented.

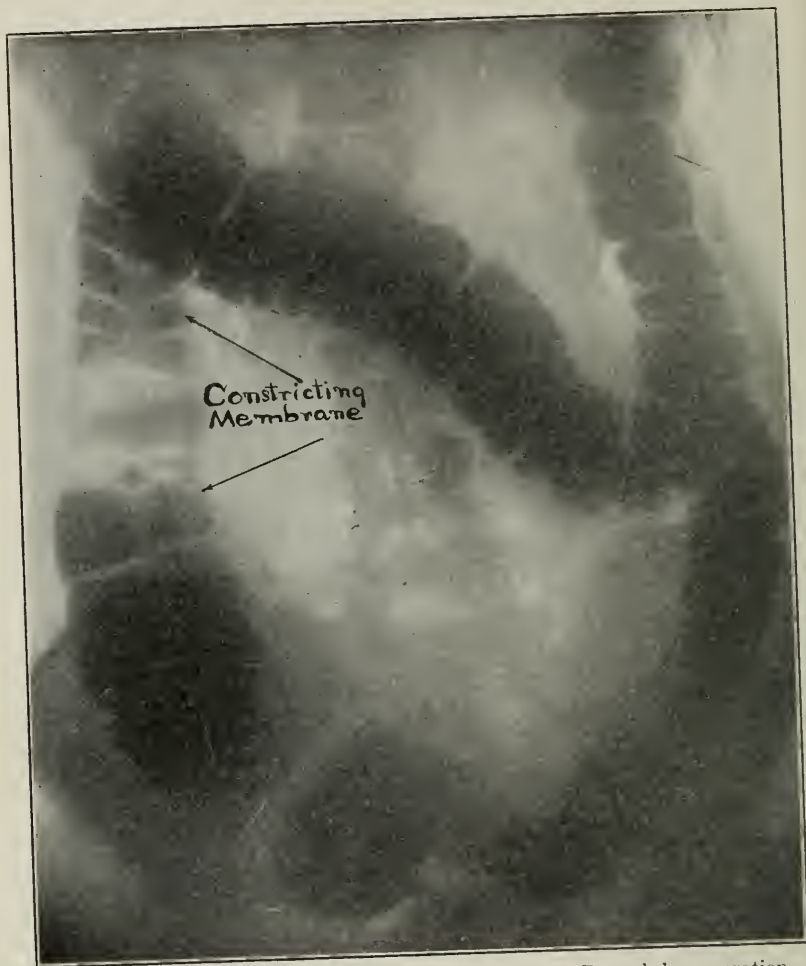


FIG. 14.—Pericolic veil, involving ascending colon. Proved by operation.

MEMBRANES AND VEILS. The various types of veils and membranes involving the cecum, ascending, and first portion of the transverse colon undoubtedly cause an iliac stasis, either directly by affecting the colon or terminal ileum, or indirectly by the associated constipation which blocks iliac evacuation. These lesions may be diagnosed with a great degree of certainty by roentgenography, preferably combined with roentgenoscopy. The drawing up of the cecum, the irregular filling defects in the colon, and particularly the "double-barrel shotgun" appearance of the ascend-

ing and first portion of the transverse colon, referred to by George, are very characteristic roentgenological findings (Fig. 14). Such conditions are undoubtedly important factors in the cause of obscure symptoms referred to the stomach and cap, particularly those associated with hyperchlorhydria, and should be searched for when the right hypochondrium fails to reveal the seat of the trouble. Sometimes the direct symptoms of constipation are so severe that the presence of gastroduodenal symptoms is entirely overlooked.

I fear that the treatment of these conditions is not so simple as some surgeons would lead us to think. One group of surgeons will split these membranes, remove the veils, and watch the colon pop out of its cage, believing that the patient is freed from symptoms forever. Unfortunately they are likely to return, renewed by the conditions which originally caused them, or by the trauma of manipulation from surgical procedure. In other cases where there is atony and dilatation, some surgeons attempt to reduce the size of the colon and hold it in position by artificially producing the conditions which the aforementioned group of surgeons try to destroy. The most successful method of surgical treatment for such cases could be determined by postoperative roentgenological investigations in conjunction with careful clinical observations.

KINKS IN THE TERMINAL PORTION OF THE ILEUM. Kinks in the terminal portion of the ileum, either with or without mobile cecum, undoubtedly do occur and cause the group of symptoms described by Lane and recognized by others. But these kinks are a rare rather than frequent cause of iliac stasis. I was told by Dr. Jordan, who has made roentgenological examinations of many of Mr. Lane's cases, that the roentgenological finding on which he bases the diagnosis of kinks of the terminal portion of the ileum is immobility of this region to palpation under fluoroscopic examination, and that the presence or absence of iliac stasis is not so important a factor. On several occasions I have been able to recognize kinks of the terminal ileum with dilatation of the proximal ileum, and I have been able to demonstrate them to even the most skeptical observer (Figs. 15 and 16). When a kink really exists and causes iliac stasis and dilatation, especially if it is associated with symptoms surgery for its relief is undoubtedly indicated. The frequency with which symptoms of these lesions are referred to the stomach or duodenum, sometimes associated with organic lesions, viz., ulcers and adhesions, as described by Mr. Lane, should be strongly emphasized. But that iliac kinks and the associated group of symptoms and pathology occur with anything like the frequency that some observers would lead us to think, or that iliac stasis is caused solely or largely by kinks of the terminal portion of the ileum, is doubtful, as evidenced by the roentgenological findings. Therefore, operative procedure intended for the relief of kinks in



FIG. 15.—Lane's kink. Proved by operation.

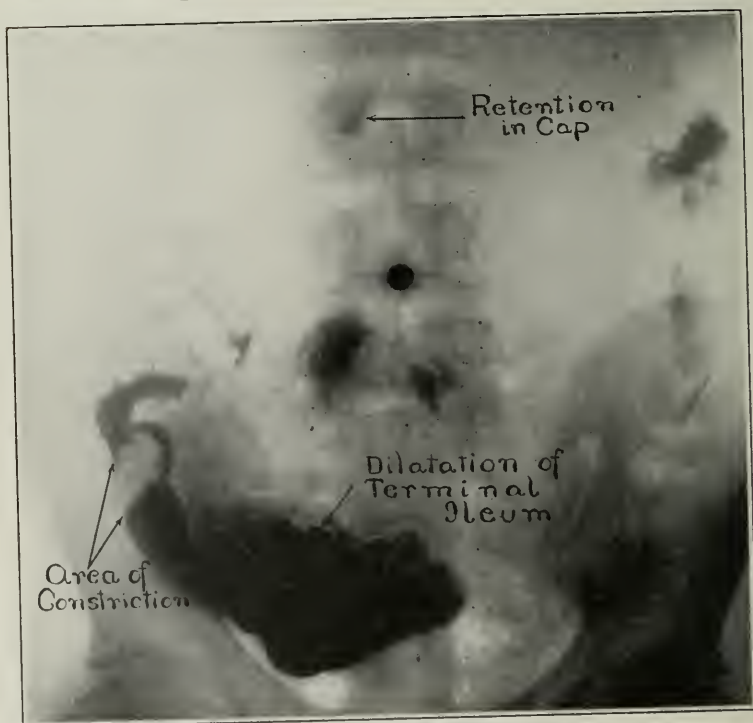


FIG. 16.—Lane's kink. Proved by operation.

the terminal portion of the ileum will not cure all cases of iliac stasis, nor relieve their associated symptoms. Furthermore, if the stasis is not caused by a kink, operative procedure may aggravate the symptoms.

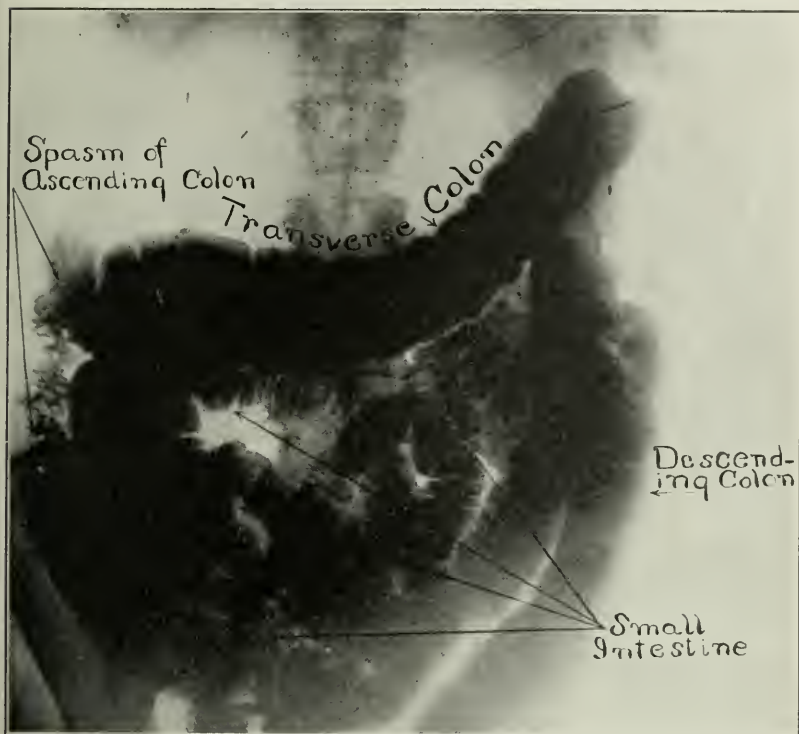


FIG. 17.—Distention of small intestine, caused by the passage of a bismuth clyster through an incompetent ileocecal valve.

INSUFFICIENCY OF THE ILEOCECAL VALVE. Insufficiency of the ileocecal valve is a condition which I first recognized in 1902 (Figs. 17 and 18). Out of the cases examined since that time I have observed about 200 cases of this irregularity, and have used every effort to arouse the interest of surgeons and practitioners in the subject without success. Even now in cases where the clyster passes all the way to the duodenum, and the patients present marked abdominal symptoms, surgeons and practitioners refuse to attribute any significance to this finding. I find that the only way I can interest them is to ask if they would expect symptoms if they fed their patients feces removed from the colon. I have failed to report this group of cases, at first because the question of tuberculosis occupied my attention, and later because my efforts were concentrated on gastroduodenal lesions. Kraus, Schwartz, Holz-

knecht, and more recently Groedel and Dietlan, have reported roentgenographical observations of ileocecal insufficiency. Case has published an article, and on several occasions demonstrated slides, showing the frequency with which this lesion manifests itself. Its clinical aspects have been described by Kellogg,⁹ who has recently devised an operation for repairing an incompetent valve, and a method of constructing an artificial one, which will undoubtedly create a great interest in the whole subject.



FIG. 18.—Distention of small intestine, caused by the passage of a bismuth clyster through an incompetent ileocecal valve.

Some of my cases of ileocecal insufficiency, particularly the first ones that I recognized as such, where the bismuth had passed a long distance up the small intestine, were associated with periodical attacks of nausea, vomiting, fever, prostration and headache,

⁹ Kellogg, Surgery of the Ileocecal Valve, Surg., Gyn., and Obst., November, 1913; Incompetency of Ileocecal Valve, Med. Record, New York, June 21, 1913.

and with cramping abdominal pain, especially marked in the right quadrant of the abdomen. This is the group of symptoms which has been attributed to a variety of causes, such as bilious attack, migraine, auto-intoxication, and frequently appendicitis. In some cases if the symptoms were sufficiently indefinite, the patient was permitted to retain his appendix, at least temporarily, in case it had not already been removed.

Reflecting on the roentgenological evidence, it occurred to me that this group of obscure symptoms was very likely due to the influx of large quantities of feces, loaded with bacteria and their products, from the colon, where they are normal, into the small intestine, which is relatively sterile compared with the colon. To increase my confidence in this theory, I found that the severity of the symptoms was proportionate to the length of the small intestine which the cecal contents traversed. Many cases were observed, presenting a mild degree of insufficiency, and the accompanying symptoms were only slight, or if acute, the attacks occurred at long intervals. Kellogg and Case have already referred to the iliac stasis, caused by or associated with this lesion, and my experience corroborates their observations.

The importance of ileocecal insufficiency justifies a communication limited to that subject alone, but it is impossible to consider it further in this communication, where it has been introduced merely as one of the potent factors in iliac stasis, and consequently in spasmodic and organic lesions of the stomach and cap.

CHRONIC APPENDICITIS. The roentgenological findings of chronic appendicitis are of immense diagnostic importance. The appendix, partially or completely filled, has occasionally been found by many roentgenologists, and reported at meetings or perhaps exhibited as a monstrosity. But Case and George deserve the credit of observing the appendix roentgenographically often enough to justify them in drawing conclusions as to the significance of its roentgenological appearance. Case states that the appendix may be shown in about 50 per cent. of the cases by milking the bismuth into its lumen. George maintains that he can show an appendix in eight cases out of ten, if it has not been removed. He finds that the appendix of a child is readily filled by manipulation, but so rapidly evacuated that it is difficult to roentgenograph it. It is doubtful if the mere filling of the appendix is of pathological significance. But as Case has already declared, much information may be derived by examining it roentgenographically. It is possible to determine its size, shape, and position, the presence or absence of areas of constriction or permanent kinks, and whether or not it is adherent to adjoining viscera. A persistent fleck of bismuth, remaining therein for several days, is an important finding, indicating incomplete evacuation. If this phenomenon is accompanied by spasmodic constriction of the cap or pars pylorica, and the

stomach, small intestine, and colon show no evidences of an organic lesion, there can be little doubt that the symptoms are due to chronic appendicitis. Even when the appendix is not visible to corroborate one's suspicions, the cause of the spasm may often be attributed to the appendix with considerable certainty, especially if the entire gastro-intestinal tract presents an otherwise perfectly normal appearance (Figs. 6 and 9).

DIAGNOSTIC VALUE OF ROENTGENOLOGY. It may be contended from a scientific stand-point that some of these deductions regarding the association of one lesion with another are not sufficiently proved. This may be true, but all inferences aside, the bare facts definitely shown by the roentgenological findings are sufficient to keep the scientific investigator busy for the next decade proving or disproving their association with each other. If our observations be correct, and we have a wealth of material to prove that they are correct, how vast is the field of functional gastro-intestinal disturbances thus opened up, whereon roentgenology is destined to throw the light which will reveal obscure lesions that have hitherto escaped detection by other methods of examination.

When the first alarm is sounded this search light should be put in action, lest, as Mayo warns, we deluge the alarm box and ignore the flames. If the roentgenologist is given an opportunity to make a complete examination, he can determine with a reasonable degree of certainty whether a torrent of surgical procedure is needed to extinguish the fire, or perhaps he may find that the chemical engine of hygiene, correct diet, and medication is sufficient. All of the lesions, with the exception of chronic appendicitis, may be diagnosed as accurately by a thorough roentgenological examination as by the old-fashioned exploratory laparotomy. Moreover, the roentgenological diagnosis can be made without loss of time or strength to the patient, and indicates whether medical or mechanical treatment will suffice or that surgical procedure is necessary.

REVIEWS

THE PROTEIN SPLIT PRODUCTS IN RELATION TO IMMUNITY AND DISEASE. By VICTOR C. VAUGHAN, M.D., LL.D., Dean of the Department of Medicine and Surgery of the University of Michigan; VICTOR C. VAUGHAN, JR., M.D., A.B., in charge of the Tuberculosis Work of the Detroit Board of Health, and J. WALTER VAUGHAN, M.D., A.B., Junior Attending Surgeon to Harper Hospital, Detroit. Pp. 476; 34 illustrations. Philadelphia and New York: Lea & Febiger, 1913.

THIS volume is a summary of the contributions of the Vaughans and their associates to the mechanism of disease. There are three distinct phases to this work:

First, the isolation of a common poisonous radical or "archon," common to all true proteins, of animal, vegetable, and bacterial origin, which they studied. This substance was not found in pure gelatin, which, it will be remembered, is a protein deficient in certain aromatic amino-acids, notably tyrosin. This poisonous deficient substance (or substances) is of unknown chemical composition, but the physiological effects produced by it in experimental animals suggest that it may be similar to or even identical with beta-imidazole-ethylamin (histamin or ergamin). Histamin may be obtained from histidin, one of the amino-acids constantly found in true proteins, by the removal of the carboxyl group. The poisonous archon, furthermore, seems to be closely related physiologically to the "anaphylatoxin" described more recently by Friedburger, and it may be synonymous with the so-called endotoxin of many bacteria. Friedburger's anaphylatoxin, the endotoxins of bacteria, and Vaughan's archon agree in one important particular: They appear to be poisonous and not toxins in the bacterial sense, that is, they do not stimulate antibody formation when they are injected into susceptible animals. True toxins stimulate antibody formation in susceptible animals under appropriate conditions.

Secondly, the effects of injecting the poisonous archon into experimental animals. Small amounts, 0.5 mg. approximately, injected intravenously kill guinea-pigs of average size within a very short time: the symptoms induced vary with the size of the dose. Fatal amounts induce symptoms essentially those described by various observers as acute anaphylactic shock, and the post-

mortem lesions are similar. The authors direct attention to the similarity of these symptoms with those following the injection of a homologous protein in a previously sensitized animal. They believe the same protein is concerned in either case.

Thirdly, the protein of the second injection in the sensitized animal is broken down *in vivo* by ferments which are elaborated by the tissue cells of the animal in response to the first injection of protein. This entire process is conceived by Vaughan to be one of parenteral digestion to free the tissues of the host from the alien protein. Among the products of the breakdown of protein in a sensitized animal is a substance resembling beta-imidazole-ethylamin. If this substance is liberated in a comparatively free state and in considerable amounts the animal dies acutely. If the protein is broken down in such a manner that this substance is liberated, combined to a greater or lesser extent with other substances, or liberated in very small amounts, the symptoms are correspondingly modified. Vaughan obtains this poisonous substance, which *in vivo* is produced by the action of specific intracellular ferments, by boiling protein with alcoholic caustic potash. According to Vaughan, therefore, the substance which he believes is closely related to beta-imidazole-ethylamin is the same as that produced in a sensitized animal following a second injection of protein and which causes acute anaphylactic death. The writers call attention to the effects of injecting protein parenterally at intervals frequent enough to prevent sensitization such injections very frequently result in the production of temperature curves and even lesions resembling strikingly those of certain of the well-known diseases, as, for example, typhoid.

These observations, and they are supported by a great deal of experimental evidence, have led to the Vaughan theory of the mechanism of disease, particularly that of bacterial causation. According to this theory, bacteria (alien protein) which develop in the tissues of the host lead to the formation of a specific ferment which will break down the protein of the bacterial bodies. During the interval which elapses between the first appearance of the bacteria in the tissues and the maturation of this ferment no clinical symptoms are apparent. This is the incubation period of the disease. When the ferment is mature it acts upon the bodies of the bacteria which are in the tissues, digests them parenterally, and liberates in greater or lesser amounts the poisonous archon. The parenteral liberation of this poison is, according to Vaughan, the factor which determines the clinical symptoms of the disease and to a very considerable extent the nature of the pathological lesions. The authors state dogmatically that the clinical and pathological manifestations of disease are attributable to the parenteral breakdown of protein (bacteria) in the tissues of the host. The nature and extent of this development and its location in the body

determine the clinical course and pathological lesions of the disease. The incubation period of a microbic disease, therefore, is that time which elapses between the initial development of the invading organism in the tissues of the host and the time required for the host to perfect a specific ferment, or perhaps ferments, to break down this alien protein. This brings the mechanism of disease into a distinct relationship with hypersensitiveness of anaphylaxis.

This work is unique and important. It places the mechanism of disease upon a chemical basis. There are two features of the theory, however, which require amplification:

First, it is rather difficult to conceive of ferment activity proceeding rapidly enough *in vivo* to effect the cleavage of the protein molecule necessary to liberate this archon in sufficient amounts within the few minutes which elapse between the injection of protein in the sensitized animal and its death from acute anaphylactic shock.

Secondly, it is not clear how the rapidly fatal septicemias in which death may occur within eighteen hours of the initial infection can be explained upon this theory.

These objections may be purely academic, however, as Vaughan has stated very definitely that much remains to be done before the entire mechanism of disease is finally elucidated. The discussion of the experimental details and the exposition of the theory which is based upon this experimental work is very clear and very direct, and this work marks an important advance in medical science.

A. I. K.

MODERN MEDICINE: ITS THEORY AND PRACTICE. IN ORIGINAL CONTRIBUTIONS BY AMERICAN AND FOREIGN AUTHORS. Edited by SIR WILLIAM OSLER, Bart., M.D., F.R.S., Regius Professor of Medicine in Oxford University, England; Honorary Professor of Medicine in Johns Hopkins University, Baltimore; formerly Professor of Clinical Medicine in the University of Pennsylvania, Philadelphia, and in McGill University, Montreal; and THOMAS McCRAE, M.D., Professor of Medicine in the Jefferson Medical College, Philadelphia; Fellow of the Royal College of Physicians, London; formerly Associate Professor of Medicine in Johns Hopkins University, Baltimore. In five octavo volumes. Second edition. Vol. I: Pp. 1093; 43 engravings and 33 plates. Vol. II: Pp. 1144; 56 engravings and 20 plates. Philadelphia and New York: Lea & Febiger, 1914.

To those who had the opportunity of observing the widespread enthusiasm and approval that was accorded the first edition of Osler's *Modern Medicine* it will occasion no surprise to learn that less than four years after the last volume of the first edition was

published the first volumes of the new second edition have begun to appear. That the entire edition of a great system of medicine in seven volumes should be so rapidly exhausted is a more eloquent tribute to the value and success of the work than any approbation which the pen of a reviewer can ever hope to bestow.

The new edition, of which two volumes have recently been issued, is new in fact as well as in name. Under the able supervision of Sir William Osler and Thomas McCrae, so much rearrangement, revision, and alteration has taken place that the new volumes deserve careful consideration and review. In the preface the editors announce that in the new edition the number of volumes is to be reduced from seven to five. This reduction has been accomplished by increasing the size of the page, augmenting the number of pages in each volume, and by omitting the introductory chapters and historical sections that appeared in the first edition, together with certain articles on subjects that have undergone little or no change during the past few years.

A comparison of the original edition with Volumes I and II of the new edition, shows that radical changes have been made in their contents and arrangement. The new Volume I is devoted to bacterial diseases, infectious diseases of unknown origin, non-bacterial fungus infections, and the mycoses. This virtually was the contents of Volume II and part of Volume III of the first edition. On the other hand, the second volume of the new edition takes up protozoan and metazoan infections, diseases due to physical agents, intoxicants, diseases of metabolism, and constitutional diseases, all of which were discussed in the first volume of the older work; but besides this the new Volume II also includes the section on diseases of the respiratory system, which occupied half of the third volume of the first edition. In short, the range of subjects considered in the first two volumes of the new edition is practically the same as was contained in the first three volumes of the original edition.

To attempt a detailed discussion of the entire contents of these volumes is perhaps unnecessary in view of the fact that the various articles are contributed by practically the same eminent group of collaborators whose names appeared in the earlier edition. Certain features in the new volume are, however, worthy of mention.

In Volume I, Hektoen's admirable article of introduction to the study of infectious diseases furnishes an excellent review of the present-day beliefs on infection and immunity. Typhoid fever is discussed by McCrae in a single chapter almost fifty pages shorter than was his original contribution of five chapters. Such condensation is typical of the new edition, and for the most part has been accomplished by shortening the etiological and pathological considerations. The original articles on lobar pneumonia were written by the late John H. Musser and George W. Norris,

whereas the present contribution is more condensed, and is by Norris alone. Three chapters are devoted to tuberculosis. Its history and etiology are discussed by Baldwin, the pathology of tuberculosis by MacCallum, while the clinical aspects of the disease are taken up by Lawrason Brown. In the earlier edition five chapters were devoted to this subject. The new article on toxemia, septicemia, and pyemia is written by R. M. Pearce and J. Harold Austin instead of by the former alone. The chapter on Malta fever, by Sir David Bruce, has been thoroughly revised by George C. Low. In this new volume smallpox, vaccination, chickenpox, scarlet fever, measles, typhus, yellow fever, etc., are grouped respectively under diseases of doubtful or unknown etiology. Councilmann's contributions on smallpox and chickenpox have been revised by E. J. G. Beardsley, and McCollom in his article on scarlet fever has been assisted by Edwin H. Place. Thomas McCrae has revised the article on yellow fever written by the late James Carroll. In this new volume the well-known introductory chapter by Sir William Osler and Professor Adami's contribution on predisposition and immunity are omitted. In spite of this omission the new volume contains 156 pages more than did the first volume of the earlier edition.

In Volume II, under protozoan infections, the chapters by G. N. Calkins on protozoa and that by L. O. Howard on mosquitoes, which appeared in the older edition, have been omitted. The subject of trypanosomiasis by Sir David Bruce has been thoroughly revised by George C. Low. The chapter on relapsing fevers, originally furnished by McCrae, has been entirely rewritten by J. Y. Todd. The chapters written by D. L. Edsall on diseases due to the various mineral and other forms of chemical poisoning have been somewhat altered and revised by Normal B. Gwyn. The section on beriberi has been largely rewritten and an entirely new chapter on pellagra added by K. Heberden Beall. Under metabolic diseases P. B. Hawk's article on general considerations of metabolism replaces the one by Chittenden and Mendel. The entire section on metabolic disorders has been revised and enlarged. The final section of Volume II deals with diseases of the respiratory system. The contributors to this group of articles are the same as in the first edition, with the exception that pneumothorax is discussed by Frederick T. Lord instead of by Walter B. James. This second volume is 316 pages larger than was the original Volume II.

Judged by these two volumes the new edition of Osler's *Modern Medicine* should prove even a more valuable and popular work than did the first edition. Thoroughly revised in every detail, printed in a larger, clearer type, and in fewer volumes, it is safe to predict that, like its predecessor, this edition is destined to occupy a foremost position among the great systems of medicine.

G. M. P.

DISEASES OF THE STOMACH, INCLUDING DIETETIC AND MEDICINAL TREATMENT. By GEORGE ROE LOCKWOOD, M.D., Professor of Clinical Medicine in the Columbia University; Attending Physician to Bellevue Hospital, New York. Pp. 624, with 126 engravings and 15 plates. Philadelphia and New York: Lea & Febiger, 1913.

THIS treatise on diseases of the stomach differs from many similar works in that it is based almost entirely upon the personal experience of the author, an experience unusually varied and extensive, embracing large groups of cases, both from hospital and private practice. The book is not chiefly a summary of other men's works and a critical review of their opinions, but is throughout an expression of Lockwood's convictions arrived at after much mature consideration and careful study of ample clinical material. This statement, however, must not be construed as implying that Lockwood has overlooked the work of others or has furnished a one-sided discussion of the subject, on the contrary, he has freely availed himself of many important statistical studies, authoritative case reports, and noteworthy pathological and experimental observations. Indeed, when the author's conclusions and the results of his experience are at variance with those of other gastro-enterologists, Lockwood shows no narrow-minded dogmatism, but frankly sets forth all opposing opinions and gives a fair and impartial discussion of the controverted subject.

Lockwood has limited his book strictly to gastric disorders, and has avoided any systematic discussion of the intestines or the accessory organs of digestion. Nevertheless, he has not lost sight of the important relationship that exists between various gastric conditions and disease of the appendix, intestines, biliary tract, circulatory and nervous systems, etc. In fact, his final chapter is devoted particularly to a consideration of this phase of the subject. He follows the best recognized pathological and clinical classifications in his divisions of the subject. He first takes up the acute inflammatory conditions of the stomach. The discussion of chronic gastritis in its various forms which follows is an unusually clear and satisfactory account of conditions which too frequently are inadequately described. In the chapter on acute and chronic ulcer and on carcinoma and other tumors of the stomach, Lockwood has taken into consideration the best present-day views of both surgeons and internists. It is gratifying to find in a book so largely medical, a chapter devoted to acute dilatation of the stomach, a subject that at one time seemed pre-empted by the surgeons. Pyloric stenosis, both congenital and acquired, is entered into with extreme care. Diaphragmatic hernia, eventration, and volvulus are accorded unusually detailed consideration. The chapter on gastropsis is a temperate and

rational presentation of a subject about which much unsubstantiated speculation and many radical opinions have often been expressed. Hyperacidity and achylia are dealt with at length and on the whole satisfactorily. The chapter on the so-called gastric neuroses, is an admirable commentary on the advances which have occurred in medical diagnosis during recent years. Whereas in older books much space was devoted to nervous affections of the stomach, Lockwood dismisses the entire subject in twenty-nine pages, in the course of which he emphatically warns that the group of nervous diseases of the stomach is a diminishing one and that the diagnosis is frequently unjustifiable and always dangerous.

Not the least useful feature of the book is the careful consideration given to treatment which is presented in detail and in a way that should prove of decided practical value. The importance of skiagraphy in gastric diagnosis is emphasized by the liberal number of excellent pictures of *x*-ray plates that suitably illustrate portions of the text.

Typographical errors are few, but they crop out here and there. For example, in the contents under Chapter X, "anatomy" should evidently be atony; again on page 190, line 15, "perforated" should be performed.

Lockwood's book is a well-balanced, interesting, and scientific account of diseases of the stomach, and should prove of great help to all who are confronted with the many perplexing problems in diagnosis and treatment presented by gastric conditions.

G. M. P.

PRINCIPLES OF SURGERY. By W. A. BRYAN, A.M., M.D., Professor of Surgery and Clinical Surgery at Vanderbilt University, Nashville, Tennessee. Pp. 677; 224 illustrations. Philadelphia and London: W. B. Saunders Company, 1913.

THIS is a small volume, which might have been made still smaller by proper condensation. It includes much more than fundamental principles, and as a consequence these very principles are not presented with sufficiently dogmatic terseness. Principles are the beginnings of things, or the elements of knowledge; among the older writers a favorite title for such a book as this is supposed to be was *Institutes of Surgery*. Certain laws apply to disease processes in general: laws of etiology, laws of pathogenesis, and laws of treatment. It is these laws which one looks to find in such a volume; but in the present volume it is difficult to find them. One might almost say that it appears uncertain whether the author has any conception of what the principles of surgery actually are.

The volume opens with a chapter of thirty pages on surgical

bacteria; but from the account given it does not appear that surgical bacteria are very different from medical or gynecological or genito-urinary bacteria, or from any bacteria about which the student learns in his course on bacteriology. The second chapter is on asepsis and antisepsis, and the third is on the process of healing. Not until the fourth chapter, and the ninetieth page is reached, is the student introduced to the first fundamental process in surgery, namely, inflammation. Inflammation in its broadest sense is the only pathological process except the growth of tumors in which surgeons have much interest; the healing of wounds, of abscesses, of ulcers, and of fractures is an inflammatory process; all surgical infections are inflammatory processes, whether caused by "pyogenic" bacteria, by bacilli of tuberculosis, by spirochetæ of syphilis or any other microbe. It seems logical therefore, to study this process before one studies its treatment; and antisepsis and asepsis are in their principles nothing else than methods of preventing and treating inflammation. It is true that the student is supposed already to have learned the pathology of inflammation in the course of his pathological studies, and that, strictly speaking, perhaps it is no more the business of a professor of surgery to teach inflammation than it is for him to teach bacteriology; but it is expedient for him to do so because in the pathological department so much stress is laid on morbid anatomy that the student overlooks the importance of pathogenesis. It is pathogenesis, *pathogenesis*, PATHOGENESIS, the course of the morbid process and *not* its appearance at any fixed stage that it is so important for the student to learn; but here again the volume now before us is lamentably weak. The pathological portions are little more than transcripts of morbid anatomy, with an occasional (an all too occasional) clinical application.

To conclude: the book is ill-balanced, not too well arranged, and though it contains much valuable information scattered throughout its pages, it also contains much matter that it is a waste of time to read, and which it was clearly a waste of time to write. It is not sufficiently dogmatic; it is a good deal too diffuse; and in few or no branches of surgery are the fundamental principles taught. For instance, in the chapter on hemorrhage the methods of applying ligatures are described (this belongs to the *practice* of surgery), but the laws (unchanged now for many years) which govern the surgeon in deciding the time, the place, and the manner of applying his ligatures are nowhere given; and in the chapter on wounds, though the method of tying sutures is described (again a point in the practice of surgery), no student will learn from this volume when to use interrupted and when continuous sutures, nor when to employ mass sutures or when to close his wound in layers.

Candidly speaking, we doubt whether this book will prove of much value to those for whose use it is designed. A. P. C. A.

SURGERY: ITS PRINCIPLES AND PRACTICE. FOR STUDENTS AND PRACTITIONERS. BY ASTLEY PASTON COOPER ASHHURST, A.B., M.D., F.A.C.S., Instructor in Surgery in the University of Pennsylvania; Associate Surgeon to the Episcopal Hospital; Assistant Surgeon to the Philadelphia Orthopedic Hospital and Infirmary for Nervous Diseases. Pp. 1141, with 7 colored plates and 1032 illustrations, mostly original, in the text. Philadelphia and New York: Lea & Febiger, 1914.

ASHHURST, in a single volume of 1141 pages, has very successfully condensed for the students' purpose the principles underlying the subject of surgery. In his preface he states that the book is written to furnish a foundation upon which a knowledge of surgery may be built. Throughout the book consistently conforms to this idea. While many of the descriptions are brief, they at least call attention to the existence of the surgical lesion in question and outline its treatment—all that could be expected of a volume of such limited scope.

The book is divided into three general headings: (1) General surgery, which is discussed in nine chapters; (2) systemic surgery, discussed in seven chapters, and (3) regional surgery, in thirteen chapters.

The colored plates and 1032 illustrations have all been selected most wisely, to illustrate certain definite types of surgical lesion or their treatment.

The first four chapters are devoted to surgical pathology, with clinical descriptions and therapeutics sufficient to supplement such pathological knowledge as the student may have, and are commendably sufficient for all practical purposes.

Chapter V is devoted to surgical technique, minor surgery, and anesthesia, and is a model of condensation.

Exception should be taken to the use of carbolic acid as a means either of skin antisepsis or in preparation of the hands, because of the dangers underlying its use and its insufficiency of action. Under the subject of skin preparation Ashhurst does not enumerate enough of the present-day methods to give an entirely satisfactory idea of the standard methods now in use.

Under the subject of aspiration it would also seem wise to have discarded the antiquated method of aspiration by the preparation of a vacuum by the suction pump, and to have substituted in its place the alcohol method of Connell and the aspiration by means of the modified Sprengle pump (Kenyon and Poole).

The portion devoted to local anesthesia is incomplete, in that no mention is made of novocain for infiltration anesthesia or tropococain in spinal anesthesia.

Chapters VI, VII, VIII, and IX are devoted to the various forms of traumatism and are sufficiently comprehensive to meet the needs for which the book is written.

Systemic surgery, *i. e.*, surgery of the blood-vascular system, bones, joints, etc., is discussed in seven chapters.

The chapter devoted to fractures is especially commendable, although it would seem wiser to have introduced a description of the moulded plaster splints of Stimson.

The chapter devoted to the diseases of bones and joints are sufficiently complete, and consist of a readable and well-classified mass of surgical data.

The chapter on orthopedic surgery is a commendable addition to a work on surgery.

The remaining chapters, XVII to XXIX inclusive, deal with the subject of regional surgery.

Chapters XVII and XVIII deal with the head and spine, and are excellent. Chapter XIX gives sufficient of the surgery of the face, mouth, and neck, and is specially well illustrated by appropriately chosen illustrations.

The surgery of the breast, chest wall, lungs, hernia of the abdomen, the gastro-intestinal tract, and the gall-bladder, liver, pancreas, and spleen are handled in a very thorough and readable manner in the succeeding chapters, and conform to the modern opinions existing concerning these regions.

It might have been wiser to have placed the chapter on venereal diseases, the surgery of the male genital organs, and the surgery of the urethra and prostate before the surgery of the bladder and kidneys, and to have included some description of the modern use of neosalvarsan in the treatment of syphilis.

The final chapter on the surgery of the female genital organs is scarcely sufficient to meet the needs of the modern student. As far as the subject is discussed it is admirably handled.

Taken as a whole the book presents a readable, accurate condensation of the subject of modern surgery, and should find a ready field of usefulness as a text-book for the student and as a handy reference-book for the general practitioner. J. M. H.

DEVELOPMENT AND ANATOMY OF THE NASAL ACCESSORY SINUSES.
By WARREN B. DAVIS, M.D.

THIS work is based on 290 lateral nasal walls, the material being obtained partly from the postmortem room of the Friedrichshain Krankenhaus, Berlin, from the Daniel Baugh Institute of Anatomy of Philadelphia, and the gynecological and obstetrical departments of Jefferson Medical College of Philadelphia. The first two chapters are devoted to the method used in preparing and obtaining the specimens and the kind of anatomical material

used. The sinuses are taken up *seriatum*, and great stress is laid upon their embryology.

There is nothing new added to what is already known concerning the anatomy of the parts, though the early development of some of the sinuses in fetal life is a distinct advance over older embryological teachings.

The 57 illustrations by Dorothy Peters are excellent in detail, being taken from the original dissections, the majority being natural size unless otherwise mentioned. B. D. P.

DISEASES OF WOMEN. By CHARLES A. L. REED, A.M., F.C.S., M.D., Professor in the University of Cincinnati; Gynecological Surgeon to the Cincinnati Hospital, the German Deaconess' Hospital, and the Jewish Hospital; former President of the American Medical Association; author of *Text-book of Gynecology*. Pp. 944; 448 illustrations. New York and London: D. Appleton & Company, 1913.

THIS volume is written, as stated in the preface, "exclusively to meet the demands of utility." And while the author endeavors by his descriptions to place the knife in the hand of the reader and direct him through the operation, he wisely cautions against the assumption of surgical skill by the book-made amateur and endorses the present movement to limit surgical practice. One feels, perhaps, that medical and hygienic measures are submerged in a descriptive maze of over two hundred operative procedures. In recognition of the wide domain of gynecology, sections are devoted to diseases of the rectum, kidney, breast, and to the surgical conditions of pregnancy and parturition. Malformations, injuries, displacements, and foreign bodies are taken up in order. The various bacterial infections receive due attention. In the treatment of streptococcic infection of the puerperal uterus, a moot point, active surgical intervention, curettage, is recommended. Emphasis is laid on the necessity of early diagnosis of malignancy, and the hysterectomy of Wertheim is regarded by the author, notwithstanding its high immediate mortality, as offering best ultimate results in carcinoma of the uterus. Radium therapy of neoplasms is not mentioned, and the use of the x-rays in treatment is dismissed in a few lines. The section on menstruation, reprinted from a former work, shows little evidence of revision. The illustrations, mostly diagrammatic, are suitably chosen to correlate the text. The index is unusually comprehensive. The volume forms a welcome addition to the literature of the subject.

P. F. W.

A HISTORY OF LARYNGOLOGY AND RHINOLOGY. By JONATHAN WRIGHT, M.D., Director of the Department of Laboratories, New York Post-Graduate Medical School and Hospital. Second edition, revised and enlarged. Pp. 357; 13 illustrations. Philadelphia and New York: Lea & Febiger, 1914.

DR. JONATHAN WRIGHT needs no introduction to any one practising the specialty of laryngology, and this book should be as well known as his earlier writings. The text of the first edition appeared in the *Laryngoscope*, but this has been greatly added to and brought up to date in the second edition. Fully half of the work is taken up with the history of the specialty from the most remote times of which we have medical records to the beginning of the last century. Much that is of interest to the student can be gleaned from these pages—interest chiefly of an historical nature. In the last half of the book, which is devoted to the development of the specialty of laryngology and rhinology as now practised, every new phase of the subject is taken up in detail and in chronological order and developed to its present status. To one interested in the history of different procedures and the question of priority in the discovery of new remedies, modes of treatment, and operation it is invaluable, as every author of note is quoted and the book thus becomes an index-medicus and a bibliography of great use to one who is engaged in literary effort. A double index of subjects and of personal names, with the bibliography of all references at the bottom of each page, immeasurably increases its value.

G. M. C.

MEDIZINISCH CHEMISCHES LABORATORIUMS HILFSBUCH. VON DR. Med et Phil. LUDWIG PINCDISSOHN. Pp. 443; 75 illustrations. Berlin: F. C. W. Vogel, 1913.

THIS work is intended to serve as a laboratory manual for medical men engaged in medical chemistry and, secondly, as a convenient reference book for more experienced physiological chemical workers. A considerable variety of subjects receive brief treatment, viz., general chemical and analytical methods, the usual examinations of urine, feces, blood, etc., some of the more difficult physiological chemical procedures even the ferments and bacteriology being touched on.

Appended are a considerable number of tables of chemical, physiologico-chemical, and more general import.

This book is to be ranked in with a number of others of the same general character and seems scarcely to show any marked advantages over many already printed.

N. W. J.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Abderhalden's Test in Epilepsy.—LERI and VURPAS (*Bull. et mém. de la soc. méd. des hôp. de Paris*, 1914, xxix, 964) raise two questions: (1) Does dysfunction of an organ necessarily cause the appearance of specific ferments in the blood, and (2), does the finding of a ferment capable of breaking down a certain tissue necessarily imply dysfunction of that particular organ? On the basis of numerous negative reactions Leri and Vurpas are inclined to give a positive "no" for answer to the first, but to the more significant second question, the study of some 50 cases failed to yield a positive answer. For instance, 25 cases of pure epilepsy yielded sera capable of breaking down brain tissue, while 10 others equally clear-cut failed to do so, results quite in harmony with those secured by Binswanger. Leri and Vurpas, however, differ from Binswanger in believing that the tissue destruction bears no constant relation to the attacks themselves, nor do they believe that sero-diagnosis will enable one to differentiate between constitutional and organic types of epilepsy. They find that the reaction is apparently not influenced by the number or severity of the attacks, the age of the patient, the age of onset or the duration of the disease. The most positive reactions took place in patients presenting outspoken mental deterioration. While Levi and Vurpas are unable to draw any valuable prognostic or therapeutic conclusions, they believe in the fundamental significance of Abderhalden's reaction.

Differential Counts of White Cells in the Counting-chamber.—DUNZELT (*Münch med. Woch.*, 1913, lx, p. 2816). Numerous attempts have been made to devise a suitable and accurate method for making

differential leukocyte counts by the use of the ordinary counting-chamber, thereby making the quantitative and qualitative study of the white cells essentially a single process. Dunzelt states that the method here described makes possible the ready recognition of all cells, normal and pathologic. Two stock solutions are required: (A) Methylene blue (Med. Hoechst), 0.08 gm. dissolved in 50 c.c. of distilled water and filtered. (B) Eosin 4 B. Hoechst 5 gm., acetone 30 c.c. and H₂O 100 c.c., filtered. To use one takes 20 c.c. of A and 40 c.c. of B: shake well and filter into a dark bottle in which the solution remains unchanged for several weeks. The ordinary blood pipettes are filled in the usual manner, the mixed solution being the diluent. Large mononuclears are readily distinguished by their size and weaker staining properties from lymphocytes which stain a deep blue. Of the granular cells, "mast cells" alone present some difficulties, often appearing, as with Ehrlich's stain, vacuolated. Nucleated red cells are easily recognized.

Complement Fixation in Gonorrhea.—THOMAS and IVY (*Arch. of Int. Med.*, 1914, xiii, 143). The report is based upon 240 cases of gonorrheal disease beside a number of cured cases, controls of a most varied type, acute and chronic urethritis, arthritis, and different types of ascending infections in women. A number of antigens were used, namely, a twenty-four-hour monovalent unfiltered antigen, trivalent and hexavalent filtered antigens, and a gonorrheal vaccine secured from Parke, Davis & Co. The first of these was made as follows: the twenty-four-hour growth on blood agar was washed off with distilled water, thoroughly shaken and allowed to autolyze for twenty-four hours at 37°, after which it was placed in a water bath at 60° for half an hour. For use it was diluted 1 to 10 with normal salt solution. Thomas and Ivy secured the following positive results: 9.9 per cent. in anterior and posterior urethritis; 21.5 per cent. in clinically cured cases; 66.2 $\frac{2}{3}$ per cent. in cases of stricture; 87.5 per cent. in epididymitis; and 100 per cent. in cases of gonorrheal arthritis. Having never observed a positive test in a non-specific case, they are inclined to regard a positive fixation as a certain indication of the existence of gonorrhea. The test is of great value in the differential diagnosis of diseases of the female adnexa. It serves as a splendid index of the results of treatment, and in chronic cases particularly gives positive results much more frequently than do either microscopical or bacteriological methods.

Congenital Hemolytic Jaundice.—CHAUFFARD (*Ann de méd.*, 1914, p. 3) cites instances to show that hereditary lues plays a distinct role in the etiology of congenital hemolytic jaundice. Thus in a man, aged fifty years, and his two daughters, all of whom had been jaundiced and anemic from birth, the Wassermann reaction was positive, and there occurred frequent attacks of pain in the region of the spleen, associated with an aggravation in the degree of the jaundice. The resistance of the red-blood cells varied from 0.64 to 0.62 per cent. NaCl. It is interesting that in 2 of the patients the injection of Salvarsan was followed by a further reduction in the resistance of the red cells and an increase in the anemia, jaundice, and hemolysins in the blood. These phenomena, regarded by the author as of the nature

of a Herxheimer reaction, were observed in another case of a man, aged twenty-two years, who also showed a positive Wassermann reaction. Latent tuberculosis also appears to have some bearing upon the disease. Thus in 3 cases that presented no symptoms, sharp reactions followed the injection of tuberculin, while in 1 case the spleen became doubled in size and the resistance of the red cells fell from 0.64 to 0.76 per cent., NaCl associated with the presence of many nucleated and granular cells in the circulating blood. Chauffard is inclined to regard hemolytic jaundice not as a disease entity but as a syndrome probably produced by numerous factors, of which hereditary syphilis and tuberculosis are at present best recognized.

Therapy in Graves' Disease.—KLOSE (*Berl. klin. W'och.*, 1914, x, 10). calls attention to the fact that while the involvement of the thymus in Basedow's disease has up to the present time served in many instances as a contra-indication for surgical procedure, today an entirely different point of view exists. It is probable that no case of Graves' disease exists without there being some involvement of the thymus at the same time, for Graves' disease is one of the entire branchial system. The degree to which either the thymus or the thyroid gland may be involved in the disease progress is a variable one, and in every case one must endeavor to decide which organ or gland in the system is the one concerned. Certainly in the majority of the cases the essential process in one of thyroid origin in which the thymus is only quantitatively affected and spontaneously recovers its normal condition, after reduction of the thyroid by operation. In a second group of cases, however, both the thyroid and the thymus are involved, and apparently in a specific sense, as seems to be shown by histological methods, though the glands themselves need not necessarily be enlarged. This type of thymus is the one most dangerous for the individual, particularly by reason of its chemical poisonous action upon the heart, especially during operations in the vicinity of the thymus, which may result in a mobilization of its toxic principle. In some of the severest cases of this type, Klose finds that the thyroid seems to be infiltrated with tissue of a thymus nature, so that he speaks of a "thymisation" of the thyroid gland. Experimentally it may be shown that such thymus glands are much more toxic for animals than are normal ones. There is yet a third group of cases in which the essential process is limited to the thymus, with practically no involvement of the thyroid. The type of thymus Basedow occurs quite infrequently, and histologically it may be shown that the thyroid is practically free from any specific changes. From a therapeutic point of view the same procedure is to be recommended in these thymus cases as is ordinarily used in the thyroid group—namely, the removal of some of the thymus itself. As yet it is somewhat difficult to diagnose clinically qualitative involvement of the thymus glands in cases of Graves' disease, but there are certain criteria which are of some help. These are a widening of the shadow in the x-ray picture of the mediastinum, the finding of myasthenia in testing the muscles with electricity and the special predominance of vagotonic symptoms in association with unusually high absolute values for the lymphocytes in the blood. Serodiagnosis by means of Abderhalden's reaction is also of great value. Absolute criteria for the

diagnosis of the specific involvement of the thymus are not yet available. Klose recommends that in all severe cases of Basedow's disease the thymus should be removed, as is done in the combined excision method at Rehn's clinic. In the last two years 200 operations have resulted in no fatal cases, and it has been striking to see the rapid improvement of the general condition of the patients and the very slight postoperative reactions which have occurred. The technique of the operation, which is easy, consists essentially in local anesthesia and removal of the thymus from its capsule, since removal with the capsule may lead to fatal hemorrhage.

Complement-fixation in Malaria.—GASBARRINI (*Zeit. f. Imm. u. exp. Therapie*, 1913, xx, 178-197). The application of the Bordet-Gengou phenomenon to the study and diagnosis of malaria has yielded some rather interesting results. The preparation of the antigen was as follows: blood was withdrawn from patients known to have abundant parasites in the circulating cells; this was well washed by centrifugalization, dried, and finally ground up into a powder. This powder finally is made up in a 1 to 30 suspension, incubated for several hours at body temperature, and the clear supernatant fluid, removed after centrifuging, is used in the test. It was found that no deviation of complement occurs when the serum is used taken during a chill or the febrile period of a malarial attack. If, however, the normal amboceptors of such sera are first removed through an adsorptive process, according to the method of Rossi and Mintz, complement-fixation occurs. It was also found that sera taken from chronic cases which had been free from attacks for varying lengths of time, gave more or less deviation of complement, even without previous adsorption. Numerous controls from normal and diseased cases gave consistently negative results.

A Case of Paroxysmal Hemaglobinuria.—WEIL and CHEVALLIER (*Bull. et mém. de la soc. méd. des hôp. de Paris*, 1914, xxx, 35), presents a case which is unusual in that it showed two distinct types of onset. The first was the usual sudden type occurring immediately after and the result of the influence of cold. The second type, though similar in its manifestations, developed only after several days, during which there were numerous prodromal symptoms, such as, muscular pains colic-like attacks in the kidney region, and extremely severe headaches. A few hours before the actual onset marked meteorism occurred, and soon after actual commencement of the attack a severe chill took place, followed by immediate improvement coincident with the passage of the first hemoglobin-containing urine. The Wassermann reaction was positive. The same was true of the Donath-Landsteiner reaction after placing the arm in iced water. It was necessary, however, to use fairly large amounts of serum not diluted with physiological salt solution nor heated to 56° C. During the actual attack there was noticed a marked acceleration of the blood coagulation as well as a lymphocytosis as high as 40 per cent., though immediately prior to the onset the polynuclear neutrophils were absolutely increased. The case also showed a complete suppression of the urinary secretion for several hours prior to the chill, followed by a polyuria. The fact that a brother of the patient suffered from the same type of disease suggests strongly that it may be an hereditary one.

SURGERY

UNDER THE CHARGE OF

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Intrathoracic Surgery.—LAPEYRE (*Archiv. d. Chir.*, 1913, vii, 1909) reviews the status of present day intrathoracic surgery. The difficulties previously encountered in making an accurate diagnosis, which should precede operation, have been largely overcome by the x-ray, and the fear of dangerous pneumothorax by various methods of artificial respiration during the operation. It is important to regard total pneumothorax as a rapidly fatal condition. Artificial respiration is not absolutely necessary in all cases, for instance in operations on the anterior mediastinum, as in operations on the heart and for tuberculous lymph nodes. The operation field in a posterior mediastinotomy is so small and deep that it is best reached through the pleural cavity, so that artificial respiration is necessary in this operation. In operating on the pleural cavity, the presence or absence of adhesions is very important. If adhesions are present, artificial respiration is not necessary, but it is absolutely necessary if the pleura is normal. The Sauerbruch chamber and Brauer apparatus are costly and little employed. The method of Meltzer is much more simple and is sufficiently dependable. Lapeyre has tried to simplify this method by interrupting the current of air being sent into the lungs by the bellows used for artificial respiration in the physiological laboratory. This method was employed in animals in four large thoracotomies (circular suture of the esophagus, pericardiorrhaphy, resection of the pneumogastries), without any disturbance being noted in the blood. He does not insist on this method but believes that with further development it can be of much value.

Post-traumatic Ossification in the Region of the Elbow-joint.—LEHMAN (*Deut. Zschr. f. Chir.*, 1914, cxxvi, 213) says that the elbow-joint, more than other joints, exhibits a predilection for post-traumatic ossification: To a certain extent this is due to its anatomical formation. These ossifications may be found after traumata of every kind, but are especially frequent after dislocations. The trauma is the determining factor. Etiologically, an individual predisposition must be assumed. The bone formation may take place from intramuscular connective tissue, as well as from the periosteum. There is practically no difference between the ossification of muscle origin and that of periosteal origin,

since both develop together. The neighboring soft tissues participate in the structure of the callus. Appropriate treatment of the recent injury is the best prophylaxis of the ossification. It involves rest and protection of the injured soft tissues, as far as possible, and the promotion of absorption. Vigorous massage and active movements are to be strictly avoided. For persistent thick infiltration, fibrolysin treatment is to be recommended. The completed ossification is capable of undergoing absorption, so that its treatment should be mostly conservative. An operation is indicated only in long continued, severe disturbances of function, and when there are complications from pressure on nerves and vessels. It should not be done before the conclusion of the process of ossification.

The Indications in Operations for Aneurysm and for Injury of the Bloodvessels.—COENEN (*Zentralbl. f. Chir.*, 1913, xl, 1913) says that whether one must treat traumatic aneurysms by ligature of the afferent and efferent branches with extirpation of the sac or by the employment of the vessel suture, and further, whether an injured large bloodvessel should be ligated or the vessel suture employed, depends on development of the collateral circulation. This should be determined before or at the time of the operation. From his experience with aneurysms in the first and second Balkan wars he developed the following method of testing the collateral circulation: Without interruption of the current the aneurysmal sac and the artery at each end are exposed. The artery is ligated above and below, close to the sac. Then below (on the peripheral side) the ligature a clamp is applied and the artery divided between this clamp and the peripheral ligature. If the clamp is now removed and bright red blood escapes from the open peripheral stump a sufficient collateral circulation is present, and one may safely apply the ligature (positive collateral sign). But if no blood escapes from the open peripheral stump, then it may be assumed, provided that a thrombus has not developed, that no collateral circulation has formed (negative collateral sign), and the vessel suture with implantation into the saphenous vein is indicated. The color of the toes or fingers help in determining the condition of the collateral circulation as well as the color of the blood which escapes from a puncture in the affected region. One cannot always wait for the stationary stage of the aneurysm nor for the complete fibrous encapsulation of the sac and formation of the collateral circulation. This is the case in war hospitals or when the escaping blood is progressively infiltrating the muscles and producing nerve paralyses. In such cases it may be necessary to operate and expose the vessels with the limb made bloodless by the Esmarch tourniquet. After clamping the vessel above and below the Esmarch band may be removed and the above test of the collateral circulation made. He operated on three stationary and four progressive aneurysms. In two, saphenous implantations were made. Gangrene did not occur in any.

Gastroduodenostomy for Ulcer.—BRUN (*Zentralbl. f. Chir.*, 1914, xli, 140) has been employing for a year gastroduodenostomy instead of gastrojejunostomy for florid pylorus and duodenal ulcer. He calls attention to the mobility of the duodenum and its availability in this

operation, but admits that, exceptionally, adhesions and inflammatory exudate will prevent the employment of the duodenum for the anastomosis. According to his experience a gastroduodenostomy for stenosis and ulcer can be performed easily much more frequently than is usually thought. He advises a vertical or, which is better, an oblique abdominal incision along the costal margin. The latter gives an excellent view of the field of operation. In simple cases with small ulcers in the anterior wall of the horizontal portion of the duodenum he usually employs a lateral gastroduodenostomy. The ulcer is turned inward by successive sutures until the afferent and efferent loops are brought together. This makes the performance of the gastroduodenostomy easier, since the stomach and mobilized, descending portion of the duodenum are already close together. Where a complete occlusion of the pylorus seems indicated, whether the ulcer is prepyloric or duodenal, he divides the stomach completely through, closes the duodenal end, and implants the gastric stump, as it is, end to end, into the descending portion of the duodenum. The anastomosis is made higher or lower according to the extent of the infiltration of the ulcer zone, or according to the desire to change the plane of the stomach. The blind closure of the peripheral lumen is safe, even when it involves the ominous duodenum, if one carefully respects its circulation. The new anastomosis removes the ulcer from the food current completely, permits the mobility, innervation, and chemistry to remain almost undisturbed, and respects the physiological principles.

Intrathoracic Goitre.—LAMSON (*Annals of Surgery*, 1914, lix, 191) reports two interesting cases of goitre extending downward into the thorax. In one a cyst developed at the lower pole. At the same time there was some enlargement of the thyroid gland in the cervical region, which about one and a half years ago disappeared, as the patient stated (probably during a fit of coughing it was drawn beneath the clavicle and was retained in the thoracic cavity). After that, beginning rather acutely, there was a marked increase in the severity of her symptoms, which were gradually growing worse. In the second case there was never any sign of any visible goitre, the growth having developed at the lower pole of the gland and extended downward into the mediastinum during the entire course of the growth, producing such marked narrowing of the trachea as to almost strangle the patient. Both patients made a complete recovery after operation.

Hematuria in the Course of Different Forms of Appendicitis.—NOVE, JOSSEAND, AND FAYOL (*Jour. d'Urolog.*, 1914, v, 121) say that hematuria may occur in all forms of appendicitis, acute and chronic, and after appendectomy. In the acute form it appears at the cessation or after the general symptoms of appendicitis. It appears suddenly without premonitory signs. It is intermittent, of short duration, and is variable in quantity. In the chronic form it precedes the appendicular symptoms proper. It occurs in patients with long-continued and variable pain in the abdomen, gastralgia, with or without vomiting, constipation, meteorism, and pains in the right iliac fossa. It co-exists with nephritic colic, confusing the diagnosis with renal or ureteral calculus, especially as lithiasis can coexist with appendicitis. Examina-

tion of the urine and cystoscopy are necessary for the diagnosis. Even *x*-rays may leave it in doubt. The hematuria is generally benign, without elevation of the temperature, or disturbance of the general condition, and ordinarily leaves no urinary sequelæ. Operation shows that frequently the appendix is in the posterior situation, adherent to the ureter and kinking it. This explains the obstruction of the ureter. In acute forms which come to autopsy an intense congestion of the kidney is found. Besides concomitant lesions of the urinary apparatus (lithiasis, tuberculosis) the hematuria can be due to general causes (nephritis) or to local causes, probably to reflex renal congestion in most cases. The appendix and ureter have a common innervation, the abdominal sympathetic. There is no treatment for the hematuria of appendicular origin in itself. It is often only a symptom of chronic appendicitis, which calls for appendectomy, after which it disappears. In the acute forms it is only a phenomenon which in itself is not an indication for operation. After appendectomy it is only a curious incident in the convalescence. In no cases do important renal lesions persist to become troublesome in the future.

Intracranial Injections for Trigeminal Neuralgia.—HARTEL (*Deut. Zeitschr. f. Chir.*, 1914, cxxvi, 429) usually uses local anesthesia with novocain by Schleich's method for the alcohol injection of the Gasserian ganglion, infiltrating intra- and subcutaneously a line from the anterior border of the ascending ramus of the lower jaw to the nasolabial groove, on a level with the upper teeth. An assistant fixes the head of the patient. The guard on the cannula is placed 6 cm. from the point, and the finger feels in the mouth, with the jaws closed, for the space between the ascending ramus of the lower jaw and the tuberosity of the upper jaw. The cannula is passed through the cheek, under the mucosa, in this space, until it strikes the smooth under surface of the temporal bone. The finger is then removed from the mouth and the glove changed. The guard on the cannula being close to the skin, is withdrawn 1.5 cm., which is the depth to which it is to be passed into the skull. With the face of the physician directly opposite that of the patient the needle is so placed that a prolongation of it would strike the pupil of the same side. The point of the needle is made to feel its way backward carefully until it is in the same plane as the articular tuberosity of the malar bone. Pain will now develop from contact with the third division of the trigeminal nerve and its branches. After some manipulation the resistance disappears and the cannula passes over the round anterior margin of the foramen ovale into the cranial cavity. Härtel says that by repeated injections with alcohol the ganglion can be made permanently anesthetic. He has employed puncture through the foramen ovale for the treatment of neuralgia, local anesthesia in large operations on the face, alcohol injections in symptomatic neuralgia from malignant tumors, for diagnosis in meningitis, and the treatment of head tetanus by intracranial injections of antitoxin. The indications for the various methods of treatment of trigeminal neuralgia are as follows: Recent cases call for laxatives and Bier's hot-air apparatus, especially the hot-air steam massage. Peripheral or central injections are also good. Chronic cases, localized to one branch, should receive peripheral basal injections. Extensive

neuralgias and those recurring after peripheral operations should receive alcohol injections of the Gasserian ganglion, which should be repeated until permanent anesthesia is obtained. In those cases in which repeated intracranial injections give no help, and in such cases where the puncture of the foramen ovale is unsuccessful for anatomical reasons, resection of the ganglion is indicated. Secondary neuralgias are to be treated etiologically. Only when due to inoperable tumors is the alcohol injection to be thought of. Hysterical cases are to be excluded so far as possible.

THERAPEUTICS

UNDER THE CHARGE OF

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The Effect of Digitalis on the Blood Pressure and Pulse Pressure in the Presence of Cardiac Decompensation.—LAWRENCE (*Boston Med. and Surg. Jour.*, 1914, clxx, 37) writes concerning the effect of digitalis when administered to patients with cardiac decompensation from various causes. He records 26 cases in detail with the effects observed from digitalis which was administered in most of the cases in the form of digipuratum. From a study of these cases Lawrence gives figures that apparently indicate that in the presence of cardiac decompensation digitalis preparations cause, as a rule, a fall in blood pressure which is usually associated with an increased urinary output. An increased systolic pressure occurs in a small number of cases and is not associated with a diuresis. It appears to him, therefore, that conditions in which an increased systolic pressure might produce untoward results do not constitute "contraindications to the administration of digitalis if cardiac decompensation indicates its use. Such conditions include arteriosclerosis, angina pectoris, and nephritic hypertension. The effect of digitalis on the diastolic pressure is similar to that on the systolic, but changes in diastolic pressure are usually of less amplitude than those observed in systolic pressure. For this reason a fall in systolic pressure usually means a diminished pulse pressure. Such a diminished pulse pressure does not necessarily mean a decreased efficiency of the circulation if the ratio of pulse pressure to maximum pressure is increased. Indeed, such a change may coincide with the increased efficiency of the circulation, as is shown by the fact that in 81 per cent. of the cases showing a fall in blood pressure there occurred a diuresis. Lawrence concludes that the effects of various drugs on the blood pressure, as determined by experiments on animals, do not furnish reliable criteria for the administration of such drugs to man. The pressure-raising effect of digitalis noted in animals and in healthy individuals does not occur, as a rule, when the drug is administered to individuals suffering from cardiac decompensation.

Serotherapy in Scarlet Fever.—Koch (*Münch. med. Woch.*, 1913, lx, 2611) writes concerning the treatment of scarlet fever patients by injections of serum derived from the blood of convalescents from scarlet fever. A mixed serum from the blood of a number of scarlet fever convalescents, free from tuberculous or luetic disease is used preferably to a serum obtained from an individual case. In 1912, Reiss and Jungmann reported 12 cases of scarlet fever treated with good results by this method and Koch adds 28 more cases in this article. Of this series, 1 patient died, but this patient was practically moribund on admission to the hospital and died one hour after the first injection. The effects of the treatment were most striking in the severe toxic cases without complications. Koch gives temperature charts in his article that seem to show the prompt action of the serum treatment upon the temperature curve. He says that this effect was parallel with marked clinical improvement in the individual cases.

The Intrameningeal Treatment of Tabes Dorsalis and Cerebrospinal Syphilis.—BOGGS and SNOWDEN (*Jour. Amer. Med. Assoc.*, 1913, lxi, 2268) report concerning the treatment of tabes dorsalis and cerebrospinal syphilis by the intraspinal injection of serum removed one hour after the intravenous injection of salvarsan or neosalvarsan. The Swift and Ellis technique was followed, except that they injected larger doses of the undiluted serum. Blood was withdrawn one hour after the intravenous administration of salvarsan and allowed to clot. The next day the serum was removed, centrifugalized, and heated at 56° C. for half an hour. Lumbar puncture was then done, cerebrospinal fluid withdrawn, and exactly enough serum injected to replace the fluid. The amounts varied between 20 and 35 c.c., and the treatment was repeated from every ten to twenty days until the spinal fluid was normal in respect to the cell-count and Wassermann. In every case there was marked improvement, the cell-count dropping to normal and the Wassermann becoming less marked and in most of the cases entirely negative. The most constant result was the disappearance of the lightning pains and other sensory disturbances, and this resulted in a more cheerful mental attitude and a corresponding improvement in the appetite and nutrition. The effect on locomotion was slower in development and less marked, but definite, and in some cases great improvement was achieved, rather more pronounced, apparently, than in patients treated by smaller doses of diluted serum.

The Benzol Treatment of Leukemia.—MÜHLMANN (*Deutsch. med. Woch.*, 1913, xxxix, 2083) reports a case of lymphatic leukemia treated with benzol during a period of nearly six months with a final fatal result. This patient had received a total of 175 gm. of benzol during this time and at the autopsy extensive necrosis of the liver was found. The patient showed marked improvement after the first three or four weeks of benzol treatment and continued to improve for two weeks after the discontinuance of the remedy. This period of improvement was closely followed by a relapse which yielded to further benzol treatment, the leukocytes dropping from 60,000 to 20,000. This temporary improvement was followed by a severe relapse while on

the benzol and the patient rapidly failed. Pappenheim has found necrosis of the liver in rabbits after the administration of benzol for continued periods of time and Neumann has also reported necrosis of the liver in a case of myeloid leukemia treated with benzol. Mühlmann cautions against the continued use of benzol in view of this apparent destructive action of benzol upon the liver.

The Scientific Basis for Vaccine Therapy.—PEARCE (*Jour. Amer. Med. Assoc.*, 1913, lxi, 2115) says that prophylactic vaccination rests on a sound scientific basis of experimental study and clinical observation. Curative vaccination has no sound experimental basis, but the application of the general principles of immunity as well as clinical observation offers a plausible basis for the treatment of localized, more or less chronic infections, and of "carriers." On the other hand, no satisfactory basis is at hand for curative vaccination in the acute self-limited diseases characterized by general dissemination and systemic infection. All attempted vaccinations in this group must be considered as purely experimental. The only logical method of vaccination is the use of "autogenous vaccines." Mixed vaccines, commercially prepared, constitute a type of bacterial polypharmacy which should be discouraged as unscientific and non-ethical. Therapeutic vaccination, if it is to be placed on a scientific basis, should be regarded as a method of treatment based on the study of the individual and his infection and not as a ready-made method capable of the universal application of stock vaccines. The use of vaccines in diseases of doubtful or unknown etiology is unscientific and ethically indefensible. Every physician practicing vaccination should bring to bear in the study of his results every method of laboratory and clinical investigation which promises light, and preferably should work with a trained immunologist. Thus only can definite knowledge of the efficacy of vaccination be obtained. It is well to remember the words of A. E. Wright in this connection. Wright asserts that for such skilled service as that demanded by vaccine therapy "is required a man who has spent years of study to master the technique, to know how to make the vaccines, to know where to look for the microbes, to know which are the most important microbes, to know how to isolate them, and, most of all, a man with sufficient experience and ability to apply all these things." In the interpretation of results it should be borne in mind that, as Theobald Smith has emphasized, vaccines rarely, if ever, cure, but act rather in aiding a process which tends to recovery by stimulating a languid process to immunization.

Splenectomy in Pernicious Anemia.—MOSSE (*Berlin. klin. Woch.*, 1913, I, 2088) describes a case with blood changes similar to those of pernicious anemia in which an apparent cure followed splenectomy. For this treatment to be successful, Mosse believes that the blood should show evidences of hemolysis. This can be determined by testing the resisting power of the red cells to salt solutions of varying strengths and to the patient's serum and alien sera. It is unusual to find evidence of increased fragility of the red cells in true pernicious anemia, as many observations have shown that the red cells in pernicious anemia are more resistant to hemolyzing agents than normal red cells.

PEDIATRICS

UNDER THE CHARGE OF

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Malaria in Infants.—WILLIAM WESTON (*Archiv. Pediat.*, 1914, xxi, 244) points out the influence of malaria on the morbidity and mortality of infants wherever the disease prevails endemically. Of the predisposing etiological factors age comes next to location. In Southern States, malaria reaches its height in July, August, and September. The pernicious types are most often seen in the early autumn. The principal forms of malaria found in the south are the tertian and estivo-autumnal. Pernicious malaria is an intensified degree of infection and not a pathological entity. In the latter condition large numbers of parasites are found in the brain at autopsy, the infantile nervous system being an important predisposing factor. The incubation period in malaria is from three to five days or less. Successive infections of tertian and quartan malaria at different periods may confuse by the attacks occurring daily. The attack usually begins abruptly with vomiting or convulsions, pallor of the skin, followed by cyanosis, followed again by reddening of the face, the nose remaining white and pinched. Temperature and pulse are high. Perspiration accompanies the fall of temperature and prostrations is severe. Infection by the estivo-autumnal type is almost always severe. Enlargement of the spleen and liver are usual, with gastro-intestinal disturbances and often acute pulmonary congestion. A diagnosis can usually be made by examining the blood taken at the beginning of a paroxysm, especially before quinine has been given. The finding of melanin in the large mononuclear leukocytes is said to be pathognomonic of malaria, but more diagnostic of chronic than acute malaria. Other valuable aids in the diagnosis are the therapeutic test, with quinine and the periodicity of the symptoms. Preventive measures, such as destroying the breeding places of mosquitoes, the screening of houses, and keeping children indoors after nightfall are highly important. Quinine bisulphate in aqueous solution is begun three hours after the child's temperature has become normal, giving 2 grains every four hours for twenty-four hours. After this period 3 grains are given morning and evening for three weeks. In pernicious malaria a 3-grain tablet of bimuriate of quinine and urea is given by means of a hypodermic syringe and injected deep in the muscles every six hours. By rectum the bimuriate is given in 6- to 9-grain doses dissolved in salt solution.

Smallpox in Infants and Children.—WILLIAM HANNA (*British Jour. Child. Dis.*, 1914, xl, 1) gives statistics of smallpox epidemics in England to show its incidence and mortality in children, and to demonstrate the fact that the prevalence of the disease has been greatly checked by vaccination. A study of the smallpox records of the Liverpool hospitals for the last ten years shows that among the

well vaccinated no cases are to be found under two years and only seven cases between two and five years of age. The immunity conferred by vaccination in infancy which protects the infant in early life, gradually loses its effect and cases begin to appear in the older children. However, these cases are never as severe as in those who never were vaccinated. No severe cases are to be found. Between two and five years 100 per cent. are very mild cases, between five and ten years 90 per cent. are very mild, and between ten and fifteen years over 80 per cent. are in the same category. Smallpox may occur concurrently with vaccinations. Concurrent vaccination, if done within the first three days of infection, almost entirely neutralizes the smallpox, so that no symptoms or signs of the disease appear or the attack will be very mild, with a few papules which do not mature but simply die away. The later in the incubation stage that vaccination is performed, the more severe the type of disease, but the disease is never more severe than of moderate severity. Vaccination performed after the symptoms have developed does not "take" typically, and the disease pursues its usual severe course. In unvaccinated children, smallpox is always severe, and the records show that up to fifteen years 80 per cent. of the cases are of the confluent type and die, while only 10 per cent. escape with a mild type of eruption. Among the vaccinated the deaths are absolutely *nil* up to fifteen years. The chief point in the diagnosis of smallpox is the relative distribution of the rash on the different parts of the body.

OBSTETRICS

UNDER THE CHARGE OF

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Cervical Cesarean Section for Double Development of the Genital Organs.—BENTHIN (*Monatsschrift f. Geburtshilfe und Gynäkologie*, 1912, Band xxxv, Heft 2), reports a case of a patient brought to clinic with beginning abortion. On examination, a double vagina was present, terminating on the right side in a retroflexed uterus in which pregnancy was developing. The vagina upon the left side was very narrow, and the cervix on the left side was but partly developed. Thirteen months later the patient again came to clinic in labor, having had uterine contractions for ten hours. The ovum had developed again in the right uterine cavity. Cultures taken from both vaginæ showed the presence of staphylococcus albus. The membranes had ruptured, the fetal head was standing transversely at the pelvic brim. After some delay the head partially descended, when progress ceased. It was impossible to bring the fetus in the axis of the pelvis, and accordingly, cervical section was performed by suprapubic incision. On

examining the tumor, the lower uterine segment of the pregnant uterus was found greatly distended. The delivery of the child proceeded without difficulty, but some delay was experienced in delivering the placenta, which was attached at the fundus. It was interesting to note that uterine contractions occurred in the pregnant uterus only, and not in the left side of the double organ. The mother recovered, but her convalescence was delayed by an attack of bronchitis. In speaking of cervical extirpation in general, Benthin states that he has performed 19 operations, with one maternal death from apoplexy in a uremic patient. He quotes Döderlein's 32 cases, with 3 deaths, and his recent statistics of 50 cases with 3 deaths. KÜSTER has operated 55 times with 2 deaths. Baisch in 16 cases saw lacerations of the perineum during operation. It is Döderlein's opinion that drainage should be employed in the connective tissue of the pelvis after this operation, as it is very difficult to secure primary union in this tissue. The entrance of bacteria into the connective tissue of the pelvis is much more serious than the entrance of bacteria into the abdominal cavity. It is important not to wait too long after rupture of the membranes, because of the danger of infection through the ascent of bacteria from the vagina into the amniotic liquid and amniotic cavity.

Vaginal Cesarean section for eclampsia is reported by BECKMANN (*Monatsschrift f. Geburtshülfe und Gynäkologie*, 1912, Band xxxv, Heft 2), he reports 43 operations, 25 on primiparæ and 18 on multiparæ. In Russian literature, Beckmann has collected in addition to his own, 53 cases. He preceded the operation by the use of the dilating bag, which greatly facilitated the procedure and made it unnecessary to open the posterior cervical wall in all but one case. In all but one patient labor was terminated by version and extraction. Forceps was used once where the head was low in the pelvic cavity. The uterus was tamponed three times to prevent relaxation. The placenta was delivered in 7 cases; in 32 Credé's method was employed, and in 4 the placenta was extracted manually. The paravaginal incision recommended by Dührssen, was necessary in but 4 among 25 primiparæ in whom the children were above the usual size. In one case the uterine wall ruptured because the dilating bag had not been sufficiently filled to procure full dilatation. Dührssen's mortality in vaginal Cesarean section was stated to be 1 per cent. In his 43 cases, Beckmann had 8 deaths, two from septic infection, a septic mortality of 4.6 per cent. By other methods of treatment in the St. Petersburg hospitals, the septic mortality of eclampsia has been 5.7 per cent. Beckmann also compares the results of conservative methods in the treatment of eclampsia prior to 1910 with prompt delivery as performed in 1910 and 1911. In the former there were 210 cases, with a mortality of 32.9 per cent. In the latter two years, 96 cases with 18 per cent. mortality. When the mortality of different methods of delivery in eclampsia is compared, it is found that the forceps had 33 per cent. mortality, spontaneous labor 10 per cent., version and extraction 14 per cent., abdominal Cesarean section, no mortality, and vaginal Cesarean section 18 per cent. It is observed that the more promptly operation is performed the better the results. The fetal mortality is also lessened by prompt operation.

The Determination of Fetal Age by the Graphic Method.—HEUSER (*Zeitschrift f. Geburtshülfe und Gynäkologie*, 1912, Band lxx, Heft 2), draws attention to Zangemeister's curves in estimating the age of the fetus. Heuser takes as important data the length of the fetal body, height of the occipitofrontal circumference of the head, the occipitofrontal diameter of the head, the depth of the head measured from the chin to the middle of the anterior fontanelle, the circumference of the breast at the nipples, the distance from the umbilicus to the breech or buttocks, the length of the legs and the length of the feet. With each measurement, so near as possible, the duration of gestation is also considered. These are all represented graphically, and their comparison to the normal enables one to judge of the degree of fetal development.

HANNES (*Zeitschrift f. Geburtshülfe und Gynäkologie*, 1912, Band lxxi, Heft 3,) writes concerning the development of the fetus in relation to the duration of pregnancy. He draws attention to the fact that the fetus at full term may vary greatly in weight and development. He finds that when the fetus is above the average in weight that considerable variation in length may be present. The average, however, in these healthy children will be from 53 to 56 cm. In cases where there was no information concerning the last menstruation, it was found that the weight of the fetus served as a constant indication of the period of gestation. In but 50 per cent. of large children was pregnancy prolonged 280 days.

The determination of fetal sex in utero is the subject of a paper by PETRI (*Zeitschrift f. Geburtshülfe und Gynäkologie*, 1912, Band lxxii, Heft 1), His method consists in the use of serum obtained from the cow and the steer, and in 7 cases where injections were made and the serum diluted from one-half to one in forty, the results indicated the sex of the child. As control, the Wassermann test was found in some cases negative, and in others positive. While the experiments gave results of interest, they were not conclusive, and could not be relied upon to positively determine the sex of the unborn fetus.

OBATA (*Zeitschrift f. Geburtshülfe und Gynäkologie*, 1912, Band lxxii, Heft 3), contributes an interesting paper upon the centres of ossification in the fetal pelvis. He finds that the centres of ossification in the ischium, pubis, ilium, first to fifth ribs, and portions of the spine, develop bilaterally during fetal life. There is unilateral development in the sacrum. All these centres of ossification seem to be composed of one mass and not of several parts. These various centres differ in length and in shape. The deposit of calcium in the ossification centres is characterized by the growth of bone cells and the gradual disappearance of the ossification centre itself. The so-called chondral reaction is found in the fetus 30 mm. long, first in the ilium, although in other bones it may be wanting. In the ilium the chondral reactions begins a short time before the deposit of calcareous material. Among many misstatements frequently made concerning obstetrics cases, that of excessive fetal size is probably the most often in evidence.

AHLFELD (*Zeitschrift f. Geburtshülfe und Gynäkologie*, 1912, Band lxxii, Heft 3), has collected previously reported cases of excessive fetal size. At the head of the list stands Ortega's case, 11,300 grams, 70 cm. long; the sex a male. Rachel and Neumer report a child 11,250

grams in weight. Beach, one of 10,750 grams in weight, in length 76 cm.; the sex a male. Olano, a female child 68 cm. long and 10,000 grams in weight. Thence the weight gradually descends to that of Baudeloque, who reports a female child 61 cm. long, weighing 6150 grams. The question naturally arises, Under what circumstances does this excessive development of the child occur? First in importance is the development of the parents. If they are excessively large and stalwart, the offspring shares in their size. There is also a tendency where the mother is well nourished to an increase in fetal size, with an increasing number of pregnancies. It is well recognized that when pregnancy occurs comparatively late in life that the tendency to overgrowth of the fetus is also present. Unquestionably the growth of the placenta and its area has something to do with this condition. The percentage of male to female children is two to one. Prolongation of pregnancy is also a cause for excessive fetal growth, which has long since been recognized. Labor is delayed in these cases because the excessive size of the head prevents its normal descent into the pelvic brim and retards labor through the absence of the pressure of the head upon the lower uterine segment and cervix. The mortality among large children is very great. In 62 cases, 50 were dead-born, three were moribund, and but nine were delivered in good condition.

VAN DER HOEVEN (*Zeitschrift f. Geburtshilfe und Gynäkologie*, 1912, Band lxii, Heft 3), contributes a paper upon breech presentation, its fetal mortality, and what can be done to lessen it. The operator has the choice of several methods: He may perform external version, converting the breech into a vertex presentation, or he may bring down a foot and extract the child so soon as the breech has been delivered, or the labor can be left to Nature alone, until the child is evidently in danger, when it is delivered. Turning the child by external version to secure a vertex presentation is rarely efficient. Prophylactic extraction of a foot is most practised by French obstetricians. The result are not good, as the head is often brought prematurely under pressure, the mortality ranging from 15 to 50 per cent. A collection of statistics upon the fetal mortality of extraction by the breech or by the feet gives figures varying from 10 to 50 per cent. Where no active interference is practiced some authorities state that 12 per cent. of cases terminate spontaneously; others more than 50 per cent. The fetal mortality in spontaneous labor in some clinics is reckoned at 0.6 per cent.; in others from 11 to 16 per cent. Where the arms and shoulders are extracted artificially, the fetal mortality varies from 3 to 13 per cent. The total mortality of children born spontaneously in breech labor varies from 8 to 24 per cent. When one strives to ascertain the reason for high fetal mortality in breech presentation, it is often found in the fact that no assistance is given to the mother until the child is about to succumb through birth pressure. The dangerous period comes after the birth of the breech. The cord is often pressed upon so severely as to produce asphyxia, and so soon as the cord is in danger of pressure the operator should immediately extract the child. The act of extraction throws the arms up and adds to the complications. Where the breech enters the pelvis spontaneously the arms remain upon the chest. In difficult cases the extraction of the breech may give rise to danger and fracture of the thigh may occur. When the foot is high up and the leg

of the fetus pressed against the abdomen, the extraction is very difficult. In delivering these cases one must remember the rule, never to interfere before the breech is born if it can possibly be avoided; but when the breech appears beyond the vulva, the child should be extracted as soon as possible. In his own experience he had lost but 5 among 126 children—a mortality of 3.9 per cent.

The Relation Between the Secretion of the Mammary Glands and the Ovaries.—COHN (*Monatsschrift f. Geburtshilfe und Gynäkologie*, 1913, Band xxxvii, Heft 1), draws attention to the relation between the mammary glands and the ovaries in both the fetus and the adult. He shows from studies in embryology that during the development of the embryo the fetus and maternal ovary exert an influence upon the development of the mammary gland in the fetus. He cites the example of a patient in whom there was a defect in the development of the uterus and vagina, the ovaries being present, and the mammary glands well developed. He also cites clinical observations to show that the enlargement of the mammary glands often observed during menstruation results from the internal secretion of the ovaries. The Fallopian tubes seem to play a negative part as regards the secretion of milk, while the action of the ovary and the milk glands of the breast seem to be antagonistic. He reports the case of a patient who had amenorrhea and atrophy of the ovaries with galactorrhea. In this case there was enlargement of the thyroid gland also. He reports also the case of a patient who received a severe burn of the thorax, arm, and upper portion of the thigh. This was followed by a very free secretion of milk in both breasts. A few days afterward menstruation developed, but to a very slight degree, followed by amenorrhea for thirteen months, during which the breasts continued to secrete abundantly. He reports experiments where the extract of the mammary gland had been injected into animals, and also ovarian extract, and the effects of this demonstrated upon the ovaries and milk glands. In some cases of endometritis and other uterine abnormalities the extract of the mammary gland has been used therapeutically to advantage. It is his conclusion that the Fallopian tubes influence the development of the breasts, but that the ovary itself has a function antagonistic to that of the milk glands.

The question of the development of sex in the fetus is discussed by WEILL (*Monatsschrift f. Geburtshilfe und Gynäkologie*, 1912, Band xxxvi, Heft 6). He attempts to demonstrate by mathematical formula that a definite relation exists between kinetic energy of the mass of cells in the embryo and its rate of change or development. He finds that the so-called generation cells of both male and female types, affect the development of the sex of the embryo. He believes that the character of nutrition and the circumstances of the mother have much to do with this. He cites the example of a nation during the time of poverty and during the prolonged war, where male children were born more frequently than female children, because during this time there was no excess of plastic proteid nutritious material; but the carbohydrates were present in considerable quantity. These afford heat and liberate force in the organism, and stimulate the vigor and movement of the male generative cells. The contrary is the case in time of prolonged peace and plenty.

The influence of the mother's age upon the sex of the child is discussed by AHLFELD (*Monatsschrift f. Geburtshülfe und Gynäkologie*, 1912, Band xxxvi, Heft 3). He believes that the proportion of male births to female increases, when the mother at the time of her first labor is either considerably below, or considerably above the average age of child-bearing.

LUTZ (*Zentralblatt f. Gynäkologie*, 1913, No. 4), presents in tabular form the characteristics of 24 infants born at nine months' gestation. The term "ripe" and "fully developed" are applied so loosely to the infant that it is necessary to have a number of points upon which to base the opinion that the child is fully developed. He would apply the term "fully developed" to a child born from thirty-nine to forty-one weeks after the first day of the last period. The term "ripe" should be limited to those children in whom development was equally advanced in all the essential points. He draws attention to the fact that an infant may be born in forty weeks after the last period and still lack some of the signs of maternity, while other children born in thirty-two weeks may seem to be fully grown. The weight, length, and the circumference of the cranium are important. The statistics indicate that at the end of the eighth month the child should weigh 2050 grams, the length should be 48 cm., and the cranial circumference 34 cm. At the ninth month 2880 grams, length 52 cm., cranial circumference 35 cm. At the tenth month, weight 3310 grams, length 54 cm., circumference of head 37 cm. Of the 24 cases cited, but three were less than 50 cm. in length.

GYNECOLOGY

UNDER THE CHARGE OF

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Endometritis and Uterine Hemorrhage.—Although the trend of modern opinion is for the most part away from the old idea that endometritis is of itself ever the real cause of excessive uterine hemorrhage, DRIESSEN (*Zentralbl. f. Gyn.*, 1914, xxxviii, 618) believes that there is one very definite type of endometritis which does stand in this relation to metrorrhagia. He also, in contradistinction to some modern authors, maintains the correctness of the older view that at each menstrual period actual bits of the surface mucosa are cast off and discharged from the uterus; this he has proved by carefully collecting and examining the menstrual blood. He believes that this occurs in the following way: In the premenstrual stage the endometrium becomes differentiated into two layers, a compact and a spongy. The former, and part of the latter, undergo necrosis, accompanied by an invasion of polymorphonuclear leukocytes. Numerous small bloodvessel ruptures, with consequent hemorrhages, occur; these hemorrhagic areas then

become organized by the ingrowth of young fibroblasts. The necrotic portions are cast off, and the newly formed stroma is covered with a new epithelium, whose cells show active proliferation. This is the normal process, and is associated with normal ovarian activity. In some cases of irregular menstruation, however, associated with an insufficiency of ovarian function—a condition that is especially apt to occur about the time of puberty or the menopause—the necrotic portions of the old endometrium are not cast off, but remain attached to the surface, just as bits of placental tissue remain after an incomplete abortion. As a result of this, Driessen thinks, a peculiar type of endometritis arises, which may be the cause of profuse hemorrhages. Pathologically, this type of endometritis is characterized by the occurrence here and there in the stroma of *hyaline masses*, the result of non-organized hemorrhages; these are always surrounded by masses of leukocytes. The glands may show some cystic dilatation, and the epithelium may be multilayered, almost suggesting malignancy. It is evident, Driessen thinks, that the presence of these hyaline and necrotic masses, acting as foreign bodies, causes the active inflammatory infiltration of the endometrium, and that the incomplete regeneration of the stroma causes compression of the gland outlets and dilatation of the deeper portions. Just as bleeding after an abortion does not cease until the placental remains are removed from the endometrium, so the menstrual bleeding associated with this type of endometritis persists until either the incompletely cast off necrotic areas are removed by curettage, or the ovarian function is completely destroyed by oöphorectomy or the x-ray. For the majority of these patients, Driessen considers the last named method of treatment the most satisfactory.

Amniotic Membrane for the Prevention of Postoperative Adhesions.

—Undoubtedly one of the most difficult problems encountered by the abdominal and pelvic surgeon is the prevention of adhesions between peritoneal surfaces from reforming after their separation, or from occurring after operations in infected areas. Many forms of artificial and animal membranes, oils, etc., have been tried, with practically no result. An interesting suggestion is now made by LYMAN and BERGTOLD (*Surg., Gyn., and Obst.*, 1914, xviii, 762) to use human amniotic membrane for this purpose. It appears to have several distinct advantages, in that it is easy to obtain in sheets of large size, it is originally sterile, can be easily preserved and kept sterile, and is thin, easy to handle, and is probably easily absorbed. Lyman and Bergtold report its use in seven cases, with very gratifying results; one of the patients was a young woman who had been operated upon twice for the relief of adhesions throughout the abdomen, without benefit. A third operation was performed, with free use of the membrane, and was followed by complete relief of the symptoms, a condition which has lasted for over five months since operation. The amniotic membrane is obtained from a patient free from constitutional disease; it is prepared by washing in running water for two hours, and is then preserved until wanted in a 0.5 per cent. solution of formaldehyde in 70 per cent. alcohol.

Disposal of Unaffected Tube in Operation for Ectopic Pregnancy.—

In order to formulate if possible some rational scheme of dealing with this often very puzzling question, R. R. SMITH (*Surg., Gyn., and Obst.*, 1914, xviii, 684) has collected from various American surgeons the records of 192 cases, all of which have been followed for at least five years after the original operation. In 48 of these patients, the operation was of such a character as to preclude the possibility of further pregnancy, and these are therefore not taken into consideration. Of the remaining 144, in whom the subsequent occurrence of pregnancy was at least theoretically possible, 47 (or almost one-third) actually became normally pregnant, some of them several times, resulting in the birth of 64 children. In 21 women a second ectopic gestation occurred, in the tube which had been left at the original operation. In 2 instances, living children were born, and subsequently a second ectopic occurred. As a result of the facts brought out in this investigation, Smith says that he has adopted the general principle of preserving the childbearing function in the younger women wherever it is at all possible to do so, even at the risk of a subsequent tubal pregnancy, but in older women, with whom the need of children is no longer so urgent, he thinks the best interest of the patient is usually served by preventing the possibility of a second ectopic gestation. He thinks that in each individual case the whole matter should be freely discussed with the patient, when this is possible, and a certain amount of weight be given to her wishes. In short, the age of the patient, the number of children she has borne, her general health, and her wishes as to further pregnancies should all be taken into consideration, and these factors should play a much more important role in forming our judgment than the gross appearance of the unaffected tube at time of operation, from which, as a rule, nothing can be told as to its future functional capacity.

Causes and Treatment of Chronic Backache.—There is probably no single symptom that appears on the records of so large a proportion of gynecological, or supposedly gynecological patients, as does *backache*. While it is undoubtedly true that in many instances the cause of this condition lies wholly within the genital organs, it is equally true that in a perhaps larger number it lies either partly or wholly outside of the sphere of gynecology in its narrowest sense. The fact, however, that in so many cases the trouble is partly due to malpositions, inflammations, etc., of the pelvic organs, and partly to other conditions altogether, should serve to emphasize that here gynecology and orthopedics approach so close as to be practically inseparable, and that the broad-minded gynecologist cannot afford to neglect wholly the orthopedic side of the question, if he would avoid the performance of many needless, if not harmful, manipulations or operations within the female pelvis. In this connection, a recent article by an orthopedist, LOVETT (*Jour. Amer. Med. Assoc.*, 1914, lxii, 1615) is of considerable interest. After eliminating tuberculosis of the spine, organic nervous disease, and the results of spinal fracture, he says that in investigating the causes of chronic backache, three etiologic classes can be identified, about which there is no reasonable doubt: (1) Disease or displacement of the pelvic organs. (2)

Traumatism to the back. (3) Arthritis of the spine. Having defined and set aside the cases belonging to these divisions, however, there still remains a large group, with regard to which there are two chief points of view, (1) that they are largely *static* in origin, due to over-strain of the posterior musculature, and (2) that they are due to a strain or relaxation of the *sacro-iliac joints*. The latter explanation, Lovett rejects for all but a very few exceptional cases. He does not consider that any x-ray or pathological evidence has ever been adduced to warrant us in believing that any considerable relaxation of these joints, sufficient to produce symptoms, actually occurs. Moreover, he does not think it possible that any of the forms of treatment commonly advocated for this supposed condition, such as elastic silk trunks, strips of adhesive plaster on the skin, a webbing belt, plaster-of-Paris jacket, etc., could possibly jam these joints firmly enough together to prevent their slipping by each other, were they inclined to do so, and the fact that in many instances these measures do give very positive relief is, in his opinion, good evidence against the correctness of the diagnosis. The majority of cases of this type Lovett believes to be in reality static in origin, due to defective lateral balance or to defective anteroposterior balance. If for any reason, one leg is longer than the other, the pelvis will become oblique, and the muscles of one side will be put under more strain than those of the other, and thus backache due to defective lateral balance arises. In cases where the abdomen is so large as to cause a serious anterior load, the anteroposterior balance may be disturbed, as well as by flat-foot, a relaxed and slumped attitude, etc. In most of these cases, relief will be afforded by correct shoes and corsets. In many of the mixed cases, *i. e.*, where the pelvic organs and static conditions appear to play a role, Lovett advises trying mechanical treatment for a time, before resorting to operation, while in other instances, in which gynecological attention is clearly indicated primarily, treatment of the static element may be subsequently necessary to produce a complete cure.

HYGIENE AND PUBLIC HEALTH

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School Diseases.—EDWIN O. JORDAN (*Jour. Amer. Med. Assoc.*, 1913, lx, 409) says there is much to favor the opinion that school attendance plays a large part, if not the chief part, in the dissemination of infectious diseases among groups of children of susceptible ages. The

school furnishes specific opportunities for infection in the friendly exchange of pocket-handkerchiefs, lead-pencils, and chewing gum. The discharge of minute droplets of spray from the mouth or nose during sneezing or coughing is also a danger difficult to guard against. The school playground as well as the school-room must be considered as having a bearing on school diseases. A wide divergence of opinion exists as to the actual proportion of cases contracted through the agency of the school. Conditions are not alike in all infectious diseases, particularly in measles, scarlet fever, and diphtheria. Investigations by Kingsford in Liverpool and Roger in America tend to emphasize the importance of school attendance in spreading measles. Scarlet fever seems to be less generally considered a school disease. Many investigations point to the milk supply as a prominent factor in spreading the disease, and there is a growing disbelief in the importance of school infection. In the case of diphtheria, while there is a difference of opinion, still there are numbers of outbreaks of the disease reported in which the connection with school attendance could not be doubted. In this disease the "diphtheria carrier" plays the important role in school infection, and when school attendance is regulated by bacteriologic findings, school epidemics quickly subside.

Reinspiration of Expired Air.—CROWDER, (*Archiv. Int. Med.*, October, 1913, xii, 420-451) has made a study of the reinspiration of expired air. By this phenomenon is meant the immediate reinspiration of a portion of our expired breath. This occurs quite commonly, in fact, may almost be regarded as a normal accompaniment of respiration during the major part of our lives. Lehman ("Der Kohlensäuregehalt der Inspirationsluft im Freien und im Zimmer," *Arch. f. Hyg.*, 1899, xxxiv, 315) and also Heymann ("Ueber den Einfluss wieder eingeathmeter Expirationsluft auf die Kohlensäure-Abgabe," *Zeitsch. f. Hyg.*, 1905, xlix, 388) determined the CO_2 of the inspired air, compared this with the CO_2 of the surrounding air, and from the difference computed the proportion of the breath which was reinspired. They found this proportion to vary greatly. It was sometimes more than 6 per cent., but dropped to zero in the open air, and in a breeze of 3 meters per second. Crowder confirms these observations and extends them much further. He shows that under many conditions the air about the face contains much more CO_2 than the surrounding air. The path of the expired air may roughly be seen by watching the course of smoke blown from the nostrils. The expired air leaves in a cone-shaped expansion, part of which lies quite close to the body, and then rises slowly by convection currents. Inspiration follows expiration immediately, therefore every chance is offered for some of the expired air to be again drawn in, except when facing a breeze of from 200 to 300 feet per minute, or when walking, riding, or fanning. When the back is turned to a breeze a little of the expired air is often reinhaled in spite of the current. The position of the head influences the amount of air rebreathed. Thus Crowder has shown that while sitting upright the reinspiration was 2.3 per cent.; lying down with a pillow tilting the head forward, 1.3 per cent.; lying flat, head thrown back, none at all. In the ordinary position in bed, with the head on the side and flexed, with pockets or dead spaces for the air to stagnate, there will

be a greater retention of expired air. This occurs especially when the head sinks into a soft pillow. It may be concluded that when one lives indoors and remains quiet he will immediately rebreathe from 1 to 2 per cent. of his own expired air; in bed it will be more, from 1 to 5 per cent., and even 10 to 18 per cent., depending on the position in which he lies. Nor does sleeping in the open insure pure air for breathing, especially when one buries his head between pillows and bedclothes for the sake of warmth. The significance of respiration and its mechanism with reference to the phenomenon of reexpiration of expired air is reviewed in a masterly way. The factor of safety indicates that slight amounts of CO_2 in excess may be compensated for and probably are not deleterious. It is again shown that a good system of ventilation requires cool, moving air with a proper humidity in order to maintain the thermic balance of the body and to stimulate its chemical activity. "A little extension of the dead space beyond the tip of the nose is of no consequence."

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Tissue Metaplasia in Grafts.—SMITH (*Jour. med. Research.*, August, 1913, xxviii, No. 3) reports the results of interchanging epithelial linings from one organ to another. Thus he grafts the gall-bladder lining upon the urinary bladder, and *vice versa*, as well as utilizing the uterine covering in both organs. The epithelium of the gall-bladder and uterus became replaced in the urinary bladder by a transitional epithelium, and the epithelium of the urinary bladder and uterus was replaced by the columnar epithelium of the gall-bladder when transplantation was made into that organ. This is doubtless due to the fact that the regional epithelium is in a better position for proliferation than the graft epithelium, and Smith does not attempt to suggest that an actual transformation from one type of cell to another occurs. When the epithelial tissue of two types is transplanted side by side into the peritoneal cavity, a cyst is formed in which both tissues independently take part, and in which neither one displaces the other. When invasion and replacement of one epithelial tissue by another takes place, as in the foregoing experiment, Smith thinks that the environmental conditions act unfavorably upon the one, and favorably upon the other. This is exactly what might have been expected; nevertheless we mention the subject because of the ingenious methods which are used to provide the proof.

The Mechanism of Lead-poisoning.—ERLENMYER (*Zeitsch. f. Exper. Path. u. Therapie*, September 16, 1913, Band xiv, Heft 2) has undertaken experimental studies for the purpose of determining whether chronic lead poisoning depends upon an accumulated mass of the metal in the body, or upon the existence of a more or less concentrated solution of lead in the circulatory cell fluids, and cell fluids in general; that is, upon the existence of what Erlenmyer calls a "lead-stream." He declares in favor of the latter, and his contention can scarcely be better explained than by giving the example of a woman who worked with cyanide of mercury and lead during an eight-and-a-half-hour day for long periods in perfect health. When her day's labor was lengthened to ten and a half hours, in three months she developed severe symptoms of chronic lead poisoning from which she recovered in the next three months. She again resumed her work at eight and a half hours per day, and during the next year remained perfectly well. The explanation was that in eight and a half hours per day she never attained the concentration of "lead-stream" which meant the minimal toxic dose, but that in ten and a half hours daily work she did. Erlenmyer has performed a large series of very painstaking experiments, and considers that the relatively insoluble lead salt enters into a solution-like relationship with the body substances, so that a lead albuminate combination is thrown into the circulation, flows through the blood, and is in part excreted through the urine and feces. Lead in such combination comes into relationship with all the cells of the organism in its way through the body, but does not tend to be retained in a constantly increasing amount. It is true that if certain organs be examined for lead, it is found, in the nervous system, for example, and in the blood and other body juices. Yet this does not mean that the metal actually enters into the cells and becomes anchored there as an alkaloid might. Nor is it likely that the lead which was dissolved, and was carried in a soluble form in the circulation, became precipitated in the individual cells, or formed a permanent chemical combination with the cell molecules. Riva has shown that in animals which had been injected with lead acetate, the lead was only found in combination with the globulins, while the nucleoproteins remained free; which seems to show that lead is actually present in solution as lead albuminate, and remains in this soluble form throughout. The element of time must also be considered in the accomplishment of a chronic poisoning by lead. Erlenmyer states that we can form a kind of ratio between the body weights and the amount of lead, and the time which elapses. He found that 1 mg. per 1000 gm. body weight produced a fatal result in fifty to sixty days, and that the minimal amount was 0.7 to 1 mg., although in certain animals more than one might be required. But the density and concentration of the "lead-stream" is more important than the duration of time. This formula was determined in cats which were injected subcutaneously with lead carbonate, and in such animals the definite, permanent retention of lead does not occur.

Tobacco and the Blood-pressure.—JOHN (*Zeitsch. f. Exper. Path. u. Therapie*, September 16, 1913, Band xiv, Heft 2) has conducted a most painstaking series of observations on the effect of smoking upon

the blood pressure. He finds that the smoking of two moderately strong cigars is sufficient to produce entirely characteristic variations of blood pressure. During the time of smoking there is a definite increase of the diastolic pressure, and a primary increase of systolic pressure, with a subsequent fall. These alterations are observable for as long as two hours after smoking has ceased. John considers that the result is brought about by the stimulation to contraction produced on the vessel walls, whereby heightened tonus is produced, a fact which has been experimentally determined. Pulse frequency is not always affected in the same way, sometimes the pulse is actually slowed, but usually there are greater variations than are to be observed in a control. Eight to ten Russian cigarettes produced the same result upon the blood system as two moderately strong cigars, and between various kinds of cigarettes very different observations were made. The observer found that even four cigars of a certain brand which he names, did not influence the blood pressure in the slightest, due probably to the fact that they are very poor in nicotine. Eight to ten cigars divided over a day are not entirely without effect upon the blood pressure; but there are so many influences that affect the blood pressure in the course of the daily life, that it is a little difficult to lay the blame definitely upon the tobacco. Cigars poor in nicotine, however, produce decidedly less effect than those which are strong in nicotine; while twenty-five or thirty cigarettes produce an effect scarcely to be distinguished from that of eight to ten moderately strong cigars. John considers that the result of his observations is that a definite influence upon the bloodvessels has been once more proved, and that nicotine is able to produce vascular changes of an arteriosclerotic nature. John goes on further to state that coronary disease should be the signal for an uncompromising attitude against the use of tobacco, and disposes of the argument that many old men with coronary disease smoke enormously without killing themselves, by stating that this does not speak for the harmlessness of tobacco, but for the enormous resistance which certain individuals possess.

Tuberculin in Healthy Animals.—KLOPSTOCK (*Zeitsch. f. Exper. Path. u. Ther.*, April, 1913, Band xiii, Heft 1) finds that repeated subcutaneous injections of old tuberculin begun at 0.1 to 5 c.c., and totalling as high as 26 c.c. for a single animal, the doses administered at intervals varying between three days and a month, gave no reaction in the majority of test animals. Six guinea-pigs out of 20 died of peritonitis. Animals so treated with tuberculin showed no increased resistance to subsequent infection by experimental means, nor did the course of the disease or the appearance of the organs at autopsy indicate any differences from control animals. The sensibility of animals first injected with tuberculin and subsequently injected by tuberculosis was found to be diminished. Repeated doses of tuberculin produced no formation of antibodies in healthy guinea-pigs.

Spirochetes.—ARNHEIM supplements his previous observations upon spirochetes, made at the Robert Koch Institute in Berlin (*Zeits. f. Hyg. u. Infekt.*, 1914, Band lxxvi, Heft 3). He used spirochetes from syphilitic material and some strains of refringens. It needs but a short period

of cultivation to develop involution forms, as well as degenerated individuals, and in cultivation the virulence falls very rapidly, so that inoculation of animals from cultivated organisms is very much the exception rather than the rule. Arnheim's experience leads him to realize that the sharp distinction once drawn between pallida and refringens are inaccurate; for in material from animals infected with pallida he finds forms so closely resembling refringens that differentiation is difficult. Insofar as agglutination and precipitation of pallida by specific sera, he found no affirmative evidence at all. Complement fixation by cultivated spirochetes in the serum of syphilitics occurs, of course, but he thinks in a lesser degree of intensity than the Wassermann reaction, and the reactions restrained by non-specific agents are rather numerous. The complement fixation reaction is not quite so dependable as the Wassermann, and both failed occasionally for unknown reasons. When cultivated spirochetes are kept in continuous contact with their poisons, Arnheim did not find that isolated individuals escaped, subsequently to multiply. Arnheim experimented also with swine pest and concludes that it is not caused by spirochetes, but that the spirochetes there discovered are saprophytic.

Lipoid Infiltration.—JASTROWITZ (*Zeits. f. Exper. Path. u. Ther.*, January, 1914, Band xv, Heft 1) publishes from Halle a very painstaking study upon the foregoing subject. The points of interest do not lie so much in the question of the amount of infiltration as the processes of synthesis by which the fat content of organs is made up from simple lipoid substances. It does not simplify the problems that in certain forms of poisoning there occurs a transportation in the blood of fat from the body depots to the great body organs; in fact, this may be so great in amount that it overshadows and hides in severe poisonings the variation in the lipoids of the organs concerned. On the other hand, however, in certain forms of poisoning, such as by arsenious acid and nitrobenzol, the fatty infiltration is slight, and the lipoids can be observed to be much increased in the blood, and in such an organ as the kidney. The phosphatids may at times in an organ be absolutely and relatively decreased, and under yet other circumstances actually increased by reason of the transport of fat by the blood; but at the same time the phosphatids relative to the total lipoids are decreased. In cases of marked fatty infiltration, the amount of lipoids is likely to be great, corresponding to the well-marked anatomical visible change; in infiltration that anatomically appears slight, it does not follow that the lipoid content is correspondingly low.

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ORIGINAL ARTICLES

SYPHILIS OF THE LIVER, IMITATING CIRRHOSIS.¹

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THAT syphilis frequently affects the liver has been known for several centuries, but no one realized how frequently until quite recent times. The Wassermann reaction in the blood has taught us the meaning of many visceral lesions whose causation was formerly obscure: some of those in heart and aorta, for example, as well as in lungs, kidneys, and brain. So with the liver, manifestations of many different types of disease are now recognized to be due to syphilitic infection, and conditions formerly considered hopeless, because there was no way known to overcome them, are now occasionally combated successfully by attacking the disease that underlies them. Rolleston in his text-book on *Diseases of the Liver* describes seven different groups of cases which syphilis of the liver may simulate: (1) portal cirrhosis; (2) lardaceous disease; (3) tumor of the liver; (4) hepatic suppuration; (5) cholelithiasis; (6) splenic anemia; (7) hypertrophic biliary cirrhosis. Among these the largest group is that imitating cirrhosis, and it is surprising how often in a case corresponding in every clinical detail to portal cirrhosis, either hypertrophic or atrophic, a positive Wassermann reaction is found and improvement and even cure follow specific treatment. A group of such remarkable instances has come under the writer's observation during the past year, partly in the medical wards of the Stanford University Medical Department and partly

¹ Read before the San Joaquin County Medical Society, October 31, 1913.
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in private work and these have prompted the decision to call attention to this subject.

CASE I.—A woman, aged forty-five years, entered the gynecological service in Lane Hospital, October 19, 1912, complaining that she had a tumor in the abdomen, which she had discovered only three weeks before. She had always previously been well, and now had no pain or discomfort except that in the abdomen. Examination showed a moderate amount of free fluid present in the peritoneal cavity, and a hard tumor in the lower abdomen, reaching as high as the navel. At operation about a gallon of clear fluid was evacuated, and the tumor, which proved to be a uterine fibroid, was removed. But it was also discovered that the gall-bladder contained gall-stones, the liver was hard and nodular, and there were numerous indurated glands in the retroperitoneal space. A piece of the nodular liver was removed for microscopic examination, and the pathologist's report on the sections read "syphilitic cirrhosis of the liver." The case was then transferred to the medical service.

The clinical feature of importance in this case was recurring ascites. Subsequent to the original removal of fluid by laparotomy, the abdomen refilled rapidly, so that three weeks later it had to be tapped and 3150 c.c. were removed. Ten days later 5400 c.c. more were withdrawn; after that the ascites never again became so excessive as to demand paracentesis. The right pleura, however, likewise gradually became filled with fluid, so that one month after the laparotomy this side of the chest had to be tapped, when 1500 c.c. were removed. One week later 1000 c.c. more were withdrawn, and only four days after that 1500 c.c. again; in each instance the aspiration of the chest was urgently required to relieve dyspnea. Always after the abdominal tapping a hard, irregular, tender mass could be felt in the right side of the abdomen, below the costal margin.

Besides the original report of the pathologist on the piece of liver tissue removed, not only the blood showed a triple X Wassermann reaction, but also the ascitic fluid and the pleural fluid when these were obtained. The combination of enlarged, nodular liver, with ascites, secondary involvement of the right pleural cavity, and such positive reactions in blood and peritoneal and pleuritic contents would have made the diagnosis sufficiently clear even without the pathologist's report.

This patient was given vigorous specific treatment. She received salvarsan intravenously in full dosage (0.6 gram) on October 27, and December 15; mercurial inunctions, 1 dram each day for thirty days, and potassium iodide in doses gradually increased from 10 grains up to 1 dram three times a day throughout her illness. But in spite of this she steadily grew weaker and thinner, and died on December 26. The autopsy showed syphilitic cirrhosis

of the liver, syphiloma at the base of the liver, and syphilitic atheroma of the aorta.

The points of special interest in this case were (1) the insidiousness of onset. The patient must have had extensive changes in her liver long before she came for advice, but never realized that she needed treatment until warned by the discovery of a tumor in her abdomen, which after all was not the real disease. (2) The finding of a hard pelvic tumor associated with ascites naturally made the surgeon think first of cancer, and when the liver was found at operation to be likewise hardened and irregular, it was supposed to be involved by metastatic growth. This possibility of malignant disease can never be overlooked when a nodular liver and ascites are combined. (3) The occurrence of right-sided hydrothorax with ascites was formerly considered almost diagnostic of tuberculosis of peritoneum and pleura, but, as Cabot has shown, this pleuritic involvement may occur secondary to ascites from any cause, even from ordinary portal cirrhosis. (4) The failure of all treatment to save this patient's life was easily understood at autopsy, when the marked changes in liver structure lay revealed, for the killing of spirochetes and checking of further ravages could not avail to restore to usefulness a vital organ already so far destroyed. But all cases have not gone so far when first discovered, and for such there still is hope, as the following will show:

CASE II.—A woman, aged forty-five years, entered the medical ward in Lane Hospital, February 13, 1913, complaining of "stomach troubles." Her general health had always been good, and she never had had any previous disease of any kind. She had been pregnant four times during her married life, but the first three had each time miscarried at seven months; the fourth pregnancy she had carried through successfully to full term, and the child was living and well. She began to ail just before Thanksgiving, 1912, with a great craving for food and water. Then she noted the following succession of symptoms: (1) Pain in the region of the navel and general abdominal distress after eating; this pain was slight and did not radiate; there was a sensation of a lump present about the navel, but she could discover none; the bowels became constipated. (2) A week or ten days after onset of these symptoms the skin became yellow, the urine dark, and the feces light colored; this jaundice persisted about a week, disappearing gradually just before Christmas. (3) She noticed about Christmas that she was losing weight rapidly, though her appetite remained good, and this combination of persistent loss of weight with good appetite had continued. (4) About January 1 she had an attack of vomiting, and noticed a small amount of blood in the vomitus; again during the night of January 30 she vomited about a pint of bright red fluid resembling blood, and the next day her stools contained dark red blood, and after that persistently resembled

tar in color and consistence. (5) Craving for food and persistent thirst had been present from the onset, so that she ate and drank large quantities, but nevertheless steadily lost in weight. The cardinal symptoms of her complaint were thus an attack of acute indigestion at the beginning, jaundice, loss of weight, hematemesis and melena, polyphagia, and polydipsia.

The woman was pale and poorly nourished. Neither the lungs, heart, nor arteries showed disease. The liver area was decreased to 8 cm.; the spleen increased to 12 cm., and the lower edge was palpable. While under observation in the ward she gradually developed marked ascites, though never excessive enough to demand tapping. The blood showed a decided secondary anemia. The urine showed a high specific gravity, and the constant presence of sugar, amounting to from 5 to 8 per cent. Finally, there was a positive triple X Wassermann reaction in the blood. The atrophic liver, enlarged spleen, ascites, with a previous history of indigestion and hematemesis, spoke clearly for hepatic cirrhosis, while the glycosuria, with polyphagia, polydipsia, and loss of weight might be explained by coincident disease of the pancreas, but both probably were luetic in origin. On treatment by salvarsan intravenously, mercury by inunction, and iodide of potassium internally in large doses she gradually improved greatly, the ascites almost entirely disappeared, and when last seen in May, 1913, though still far from well, she was able to get about all the time and to attend to her household duties.

While the foregoing cases were undoubtedly cirrhosis of the liver, but a special form of cirrhosis due to syphilis, it must be remembered that not all conditions resembling by clinical and by laboratory tests those described are necessarily cirrhosis or due to lues. The old observation that in clinical medicine two and two do not always make four is demonstrated by the following history:

CASE III.—A man, aged fifty-five years, entered the medical ward on March 18, 1912, complaining of jaundice that had existed since the previous January. He had never been ill before. The present trouble began with severe diarrhea, persisting for a week, followed by slight jaundice, which rapidly deepened. He had since been given a limited diet, and to this attributed the fact that he had lost twenty pounds in weight. He had no subjective symptoms whatever. His appetite was good; digestion undisturbed; there was no pain in the abdomen or elsewhere, and no marked loss of strength. Examination showed extreme jaundice; a large, hard, smooth liver, measuring 13 cm. in area in the nipple line, and palpable for 8 cm. below the costal margin, with the lower border sharply defined; and an enlarged spleen with lower border palpable below the left costal margin. The liver was not particularly tender and not nodular. No other physical abnormalities were found, in the remainder of the abdomen or the rectum, to account for the jaundice.

The blood showed a triple X Wassermann reaction and combining this with the clinical history and physical findings a diagnosis was reached of syphilis of the liver. He was therefore given salvarsan intravenously on two different occasions, with an interval of two weeks between doses, followed by a course of mercurial inunction and by potassium iodide internally. But this treatment had no effect whatever upon his jaundice or upon the size of his liver or spleen. On the contrary, he steadily grew weaker, and ascites gradually developed. Therefore, on April 24 an exploratory laparotomy was done by Dr. Stillman, and this revealed at the upper border of the left lobe of the liver a hard, nodular mass as large as a man's fist. As this was considered inoperable, the abdomen was closed at once, but the patient died a few days later, on April 27. The autopsy disclosed a huge carcinoma of the liver, with central degeneration. No primary focus could be found elsewhere, after careful search, and the case was set down as one of primary hepatic carcinoma.

It seems probable that there was no relation whatever between this patient's real disease and his Wassermann reaction. The latter was undoubtedly evidence of syphilitic infection, but it did not give any reliable clue as to the nature of the pathological process in the liver; the two conditions were present simply by coincidence and not at all as cause and effect. It is possible, of course, that ordinary portal cirrhosis and a Wassermann reaction may in the same way coexist in a patient without meaning that the cirrhosis is luetic; but when a marked beneficial effect from therapy directed to syphilis is produced upon the symptoms and signs due to hepatic disease, the conclusion seems warranted that the coexistence of the two is more than a coincidence. Such was the conclusion in Case II, and such seemed clearly to be the case in the following instance.

CASE IV.—In June, 1913, a man, aged fifty-three years, sought advice for "stomach trouble." He had never had any previous illness of consequence, except he recalled a venereal sore when he was eighteen, which was treated briefly and "cured." Since then he had remained perfectly well until the present trouble began. He had been ailing about eighteen months, complaining at the outset for months of vertigo like seasickness, so that for days at a time he would have to remain in bed. Recently this symptom had been less troublesome; but he complained particularly now of soreness, and tenderness over the pit of the stomach; and if he lay on the left side, he felt so much pain he had to turn back to the right. Appetite was good; he felt hungry all the time; his food did not distress; there was no nausea nor vomiting. He had lost about thirty-five pounds in weight, and had grown very weak; also, he had noted that in the last few months he had grown pale, sallow, and icteric. This patient had a greatly enlarged liver, palpable

across the upper abdomen, with a total area on percussion of 16 cm.; the lower edge was hard but rounded, and the surface smooth and regular, but quite tender. There was no ascites, and no other organic abnormality was found. The blood showed a triple X Wassermann reaction. After treatment by mercurial inunctions and potassium iodide internally (the patient declined salvarsan), this patient in three months gained twenty-two pounds, his liver dulness receded until it measured but 10 cm., and his symptoms all disappeared.

Here was a case of undoubtedly hepatic syphilis, not yet having reached the stage of ascites, marvellously improved by specific therapy. Its recognition by means of the Wassermann reaction clearly indicated the plan of treatment, and the treatment proved by its efficacy that the hepatic cirrhosis and the luetic infection were sequence and not coincidence.

But the recognition of cirrhosis of the liver does not always lead to a test for syphilis as a possible cause, and so valuable time may be lost and a true understanding of the facts comes too late. The following case is one that might possibly have been saved had it been estimated earlier at its real value.

CASE V.—In August, 1913, a man, aged fifty-four years, was brought to Lane Hospital delirious and unconscious. Through his friends it was learned that he had always been well until a year before, when he vomited a quantity of blood; and since then he had gradually "run down," growing steadily thinner and weaker and less and less able to attend to his work. Two weeks before coming to the hospital he grew so weak he had to go to bed, became drowsy and delirious and remained so from that time on. On examination he was found to be greatly emaciated and slightly icteric; there was a moderate ascites, with atrophied liver and enlarged spleen; no signs of disease in the heart, but dulness and rales at each pulmonary base; the urine showed a heavy cloud of albumin, with many hyaline and granular casts. He was found to have a daily persistent rise of temperature, from 100° each morning to 103° each afternoon; his blood showed 21,600 leukocytes to the cm., with 88 per cent. polymorphonuclears. After coming to the hospital he lived but three days. The diagnosis made was cirrhosis of the liver, with ascites and with terminal toxemia. The report on the Wassermann reaction was not received prior to death. Autopsy revealed a liver shrunken to half its normal size, nodular and irregular, with many fibrous strands running through it, and a spleen about twice the normal size, studded with small abscesses, subsequently proved to be broken-down gummata. Both lungs showed a terminal pneumonia, which was the direct cause of death, and which accounted for the toxemia, the fever, and the leukocytosis.

If this man's condition had been recognized a year earlier, when he had his hematemesis, there would have been some prospect of

saving his life. Even then, however, the diagnosis would probably have been simply cirrhosis of the liver and the real etiology would have escaped notice, for there was nothing in the man's past history, his manner of life, or his previous ailments to cause any suspicion whatever of lues; if one depended only upon old routine methods of investigation, no other conclusion than cirrhosis could have been reached.

The final case observed illustrates how the error of overdiagnosis may be made and a conclusion reached that is even more serious than the facts warrant, rather than less so.

CASE VI.—A woman, aged forty-three years, was brought from the country in September, 1913, for examination, because her husband had been told she had cancer and her case was hopeless. She had been married for twenty-six years, but never had a pregnancy. Though always of small frame and low energy, she had never had any serious disease. For eight years she had had chronic "stomach trouble," her food souring soon after it was eaten, with occasional vomiting of material very irritating to the throat, and her sleep habitually disturbed by gas in the stomach and distress. She never had weighed over one hundred and twelve pounds, but there had been no recent loss of weight of any consequence. The patient was small, poorly nourished, pale, and sallow. No abnormality was found in any organ except in the abdomen; but there was found a marked bulging over the right lower thorax and upper abdomen; dulness on percussion from slightly below the nipple level to the level of the navel, 21 cm. in all; the lower border of this mass was palpable as a sharp, hard edge; the surface smooth but very tender. The spleen apparently was not enlarged. The abdomen showed a small amount of free fluid present. The stomach was displaced downward but not dilated, with no evidence of food retention, and a moderate subacidity; total acidity, 30 per cent.; free HCl, 12 per cent.; combined HCl, 10 per cent. The Wassermann reaction was a triple X positive one. On these findings it seemed reasonable to assume that her true condition was hepatic syphilis and not cancer. Too short a time has since elapsed to put the matter to the therapeutic test.

CONCLUSIONS.—The lessons to be learned from the foregoing histories are the following:

1. In any case that appears to be cirrhosis of the liver, judging from clinical history and physical signs, the blood should always be examined for syphilis. If the Wassermann reaction is positive, vigorous specific treatment will often produce marvelous improvement not to be expected in any other way; but even when the reaction is positive, the liver disease may not be luetic, and so specific therapy may prove of no avail; yet at the same time the therapeutic test will have given valuable information and have done no harm.

2. There is no certain way to tell which case of hepatic cirrhosis is luetic and which is not, except by the blood test, for previous history of infection, or of other earlier manifestations of syphilis, as well as stigmata produced elsewhere in the body by the disease, may all be lacking absolutely; while there may be nothing about the condition of the liver on physical examination or the symptoms it produces, to determine the etiology or to distinguish ordinary portal cirrhosis from luetic.

3. Syphilitic cirrhosis of the liver is a common form of hepatic disease, and must never be forgotten in the differential diagnosis of any case where symptoms and signs point to the liver as the organ involved.

SYPHILIS OF THE VERTEBRAL COLUMN: ITS SYMPTOMATOLOGY AND NEURAL COMPLICATIONS.¹

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INTRODUCTORY REMARKS. Syphilis is recognized as a fairly frequent occurrence in certain portions of the skeleton, more especially of the tibia, clavicle, and skull. All authorities agree that involvement of the spinal column is very rare, and some writers even regard its occurrence in the dorsal and lumbar regions as somewhat doubtful. This spirit of skepticism is probably due to the fact that many of the cases formerly recorded as syphilitic were really tubercular in nature, and many such errors of interpretation are to be found in the earlier literature. In the past few years, interest in this question has been revived, and the condition while unquestionably more frequent than is generally held, is nevertheless a comparatively rare affection.

At the present time, there are about one hundred well-authenticated cases recorded in literature, from which may be obtained a fair idea of its frequency, localization, and symptomatology.

The first statistics on this subject were published by Neumann in 1904, giving an analysis of 55 cases. The vertebral localization was as follows:

Cervical region	36 cases
Dorsal region	9 "
Lumbar region	8 "
Sacral region	2 "

¹ Presented at the meeting of the American Neurological Association, June, 1912.

Of the cervical group, in all but 8 cases, the disease was localized in the four upper vertebræ, a majority of these involving the axis and atlas.

Petren, in 1909, again analyzed the existing cases, and in his series the same frequency of involvement in the cervical region is shown:

Cervical region	42 cases
Dorsal region	6 "
Lumbar region	4 "
Sacral region	3 "

Ziesche, in 1911, collected 88 cases, distributed as follows:

Cervical region	61 cases
Dorsal region	12 "
Lumbar region	5 "
Sacral region	2 "
Cervical and dorsal region	1 "
Dorsolumbar region	3 "
Diffuse	4 "

In this series the number of vertebræ affected in a given case was also tabulated, which shows a decided tendency to limitation of the process within a circumscribed area.

NUMBER OF VERTEBRÆ INVOLVED.

1 vertebra in	25 cases
2 vertebræ in	17 "
3 vertebræ in	11 "
4 vertebræ in	3 "
Diffused in	4 "

Cases of syphilitic disease of the spine have also been recorded by Fry and Sachs in this country, which with 4 personal observations and those of Oppenheim not included in the previous statistics, bring the total number of available cases up to 100.

The great frequency of the cervical localization has been noted by all writers on this subject. Gerhardt has suggested that this frequency may be due to the proximity of this region to the bones of the skull, and as a consequence the extension of the disease downward. Another potent factor has been the secondary involvement of the upper cervical vertebræ by direct extension from pharyngeal ulcerations and gummata. This is especially true of the older cases, in which sequestra and fragments of necrosed bone having this origin were not infrequently expelled through the mouth. Neumann regarded the extension from pharyngeal ulcerations as the chief cause of cervical involvement in the majority of cases.

That the dorsal region may also be the seat of the lesion is shown conclusively by one of Oppenheim's cases, with involvement of

the eleventh and twelfth dorsal vertebrae and spinal-cord complications, as well as a more recent observation by Preiser. In Case IV of my series there was syphilitic osteitis of the lower lumbar vertebrae and sacrum, confirmed by pathological examination.

The x-rays will probably play an important role in the future diagnosis of this disease. In one of Petren's cases the diagnosis was confirmed by this means, and Sachs has emphasized the importance of this method.

In two of my cases with severe vertebral symptoms, no bone lesions could be demonstrated in the radiogram, and the bone involvement was evidently more in the nature of a periostitis (perispondylitis). In another, however, definite lesions, exostoses with thickening of bone tissue, were found.

The pathological lesions in the vertebral cases are the same as are found elsewhere when the skeleton is involved, and consist of exostoses, gummatous periostitis, and osteomyelitis, with occasional necrosis and sequestration of bone. The tendency to pus formation is slight, and "cold abscesses" as found in tubercular caries apparently do not occur.

It is evidently rare for the spine to be affected in the second stage of syphilis, the greater number originating in the tertiary period. Petren has described a case occurring in an infant with secondary lesions. Neumann maintains that hereditary lues may be localized in the spine, and records four cases between the ages of four and eleven years.

The *symptomatology* of syphilitic spondylitis does not differ essentially from that accompanying other affections of the spine, and consist essentially of pain, tenderness, rigidity, and deformity. In some cases, more especially in the cervical region, firm, nodular swellings may be palpated (exostoses). Tenderness appears to be more marked than is usual in tubercular spondylitis, and the nocturnal osteocopic pains are particularly persistent and distressing.

In cervical involvement it has been remarked by Petren and also by Ziesché that rotation of the head is more restricted than flexion; the reverse was true in one of my cases.

One of the most interesting questions of symptomatology is the frequency and nature of neural complications resulting from invasion or compression of the spinal cord and nerve roots. Of the 100 cases which I analyzed, neural symptoms were present in 26, distributed as follows:

Cervical region	15 cases
Dorsal region	5 "
Lumbar region.	4 "
Sacral region	2 "

It is to be remarked that neural symptoms are increasingly more frequent in the recent reports, doubtless due to the more

technical methods of the present day, which serve to detect the milder grades of pressure both of the cord and nerve roots.

The neurological examinations in this series of cases are by no means complete, so that a detailed analysis is impossible, but a general idea may be obtained of the nature and extent of the injuries sustained by the neural structures.

Of the 26 cases with neural complications, 14 were associated with symptoms that would indicate a lesion of the spinal cord, corresponding to the level of the bone disease, a "compression myelitis," in the sense in which this term is used in caries.

In 9 cases the limitation of symptoms to paralysis and paresthesia of one upper or lower extremity indicated a radicular origin. Such an involvement of the roots or plexus producing monoplegia alone must be a rare occurrence in Pott's disease, and when it is present should arouse the suspicion of syphilis.

In 2 cases of sacral origin the symptoms indicated an involvement of the strands of the cauda equina.

An unusual complication occurred in Case III of my series, a cervical spondylitis, with symptoms indicating a lesion of the medulla oblongata, possibly from involvement of the vertebral artery as it courses through the transverse processes in the neck.

Of special interest is the occurrence of root pains, paresthesia, and localized paralysis of an extremity corresponding to the region involved. This group of cases is particularly frequent in the cervical region, and may simulate pachymeningitis cervicalis hypertrophica. Sachs especially has emphasized this resemblance, and advocates the x-rays as an important means of differentiation.

Similar cases are also met with in the lumbar region, and may be unilateral or bilateral in distribution, due to involvement of the nerve roots or adjacent plexus.

It is interesting to note in passing that parasymphylis may also be complicated with syphilitic spondylitis (Hallopeau and Sachs).

Of special complications which may occur the most noteworthy is ulceration of the pharynx which was observed in 16 cases of the cervical localization (Neumann), and which gave rise in 9 cases to extrusion of fragments of necrosed and carious bone. Sudden death has occurred from erosion of the vertebral artery (Mackenzie), and once from ulceration and rupture of the internal carotid (Landrieux).

In common with diseases of the upper cervical vertebrae, the odontoid process may undergo spontaneous fracture with compression of the cord.

REPORT OF CASES.

CASE I.—*Syphilis of the skull (exostoses) and knee-joint, and syphilitic laryngitis preceded the development of vertebral symptoms;*

these came on suddenly in the upper cervical region, simulating rheumatic myositis; x-ray examination was negative; girdle pains around the base of the neck and lancinating pains in the distribution of the occipital nerves were the only nerve complications; gradual subsidence of pain under antisyphilitic treatment; rigidity persisted for some months, but gradually disappeared with complete restoration of functions.

History. The patient, a man, aged forty-three years, an expert accountant by occupation, was referred to me on April 7, 1910, by Dr. Frank W. Murray, for severe headache which had persisted for over a year. He had pneumonia at the age of seventeen years and typhoid fever at thirty-two years, following which there was slight deafness with occasional tinnitus in the right ear. He is moderate in the use of alcohol, and denied emphatically any venereal disease. One brother died of tuberculosis, but this is the only occurrence in the family history worthy of special mention.

In January, 1909, he had a throat trouble, accompanied by huskiness of voice, which was diagnosed as a possible tubercular lesion of the larynx. His family physician, however, suspected syphilis, and under moderate doses of potassium iodide all symptoms disappeared. Coincident with the laryngitis there developed frontal and temporal headaches, which were always most severe at night, and these have continued with occasional remissions up to the present time. Because of the nocturnal character of the pain it was his custom to sleep during the day, as sleep at night was impossible, owing to the intense pain. He had noticed that while taking the potassium iodide the headaches seemed less intense, but this treatment had been intermittent, and the drug had never been taken continuously or in large doses. After a time three small round prominences appeared on the left frontal bone (exostoses). He stated that in the autumn of 1908 he had had pain and swelling of the left knee-joint, which gradually subsided. At the present time the knee-joint is swollen, and there is a slight effusion in the joint; there is also a very tender point over the patella. He has never had any vomiting or vertigo with the headaches, which were distinctly nocturnal and osteoscopic in character. There were no other cerebral or nervous symptoms present.

Status Præsens. April 7, 1910. The pupils are equal and react promptly. No tremors. Skin and deep reflexes are normal, as are the cranial nerves. The deafness on the right side is of the middle-ear type. Optic disks are normal. Urine is normal. Examination of the viscera proved negative. The Noguchi test of the blood gave a positive reaction. Corresponding to the site of one of the small projections of bone noted by the patient in the left frontal region a small depression in the skull can now be palpated. Clinically the case is clearly one of bone syphilis involving the cranium and the articulation of the left knee-joint. He was

placed upon ascending doses of iodides, with hypodermic injections of the salicylate of mercury.

May 12. Under mixed treatment the headaches promptly ceased; the swelling of the knee-joint subsided, but has not entirely disappeared, and he still has occasional pains in the joint.

June 30. There is still slight swelling and some tenderness of the knee-joint. No cranial pain.

August 1. Owing to intestinal symptoms, the iodides and mercury were omitted.

September 1. Pains in the knee and skull have entirely disappeared. Wassermann reaction was strongly positive. He was told that he unquestionably had syphilis, and should undergo a prolonged and systematic course of treatment. He did not take this advice seriously, and did not return until January 21, 1911, when he appeared with a puffy edema over the right eye, which had developed suddenly and under which the bone was tender to pressure. There was little or no spontaneous pain. He had had no antisyphilitic treatment since the previous July.

The swelling subsided rapidly under antisyphilitic treatment, after which he did not return until October 12, 1911. At this time he complained of no symptoms, and the Wassermann reaction was negative.

October 16, 1911. He returned with a painful and stiff neck of three days' duration, which had appeared suddenly after sitting in the open air for two hours in a strong wind, watching a base-ball game. He had with it a sore throat and a general feeling of having taken cold. In view of the negative Wassermann reaction on October 12, and a very clear history of exposure to cold with sore throat, he was placed upon antirheumatic treatment, although with the previous history the possibility of lues was held in reserve. As little or no improvement followed the usual local and general treatment for rheumatic myositis, he was again placed upon antisyphilitic treatment.

November 1. At this time the movements of the neck were restricted in all directions, and caused considerable pain (see Fig. 1). There was distinct tenderness over the second and third cervical vertebræ, also on deep pressure on both sides of the spinous processes. Opening the mouth caused sudden pains in the occiput. There has also developed a tender and painful spot over the right parietal bone. Sharp, shooting pains are felt in the course of both occipital nerves. He also complained of a tight band-like drawing sensation around the sides and base of the neck (neck girdle). Swallowing caused painful sensations in the lower occipital region. Pain is much worse at night, coming on about five o'clock in the afternoon. In the morning he is fairly comfortable.

November 11. Movements of the neck are a little less restricted. The second cervical segment is still tender on pressure. Girdle

sensation is also present about the root of the neck, and jarring of the spine causes shooting pains in the right occiput and auricular region. The painful spot over the parietal bone is still tender.



FIG. 1.—Syphilitic spondylitis of cervical region. Case 1. Patient picking up an object on the floor, showing marked rigidity of the neck and fixation of the head.

x-ray examination by Dr. L. G. Cole, who reports as follows: "Structure and contour of the bones of the head and neck show distinctly. Bodies of vertebra and intervertebral foramina are quite distinct. In the lateral direction the bodies of the third, fourth, and fifth vertebrae are normal in size, shape, and alignment. There is an unusual space between the anterior ring of the first vertebra and the body of the second vertebra, and the relation of the odontoid process to the anterior ring of the first cervical vertebra is altered. In addition there is a spur on the upper surface of the ring which forms the partial foramen through which the first nerve emerges from the spine. This spur is to be regarded as an anomaly. Otherwise the examination is negative. I am unable to detect any change in the structure of these bones which would indicate that it is of syphilitic or tubercular origin.

November 17. He is generally free from pain in the early part of the day, but it returns about four or five o'clock in the afternoon. It is burning and throbbing in character. The neck is much more flexible, especially backward and forward. It is, however, held stiffly. Tenderness of the second and third cervical vertebræ has practically disappeared. Jarring of the spine causes shooting pains over the mastoid on both sides.

January 19, 1912. A second *x*-ray examination was made by Dr. E. W. Caldwell, who reports as follows: "I made a number of *x*-ray plates showing the lower six cervical vertebræ very well. I do not find any indication of the cause of his symptoms, in this part of the column, but I suspect that the trouble is in the articulation between the axis and the atlas, the shadow of which is obscured by the shadow of the skull. The limited rotation in this joint makes it practically impossible to secure an *x*-ray shadow of it which is not obscured by superimposed shadows of the other bones."

March 5. Neck is still stiff, but has steadily improved. The lateral movement is more restricted toward the right. There is still some deep-seated tenderness over the second and third cervical spines.

REMARKS. Under the continuation of antiluetic treatment, pain and tenderness entirely disappeared. For some months the movements of the neck were restricted, especially flexion and extension, but after a course of osteopathic treatment (taken on his own initiative) this rigidity entirely disappeared. He is still unwilling to believe that the disease is syphilis, and now that he is well he is averse to taking further precaution or treatment.

The onset of vertebral symptoms in this case had been preceded during the previous three years by a train of symptoms clearly indicating syphilitic involvement of the cranial bones, the knee-joint, and the larynx. All of these various manifestations subsided under antiluetic measures. While a specific infection was denied, the Wassermann was positive. From these clinical facts there can be no question as to the syphilitic nature of the subsequent symptoms in the cervical region. The process was apparently localized in the upper three cervical vertebræ, judging from the local tenderness, which was quite marked, and the root pains and girdle sensations of the neck which corresponded to these levels. There were no symptoms pointing to involvement of the spinal cord.

One of the interesting features of the case was the sudden onset following exposure to cold, so that the clinical picture closely resembled rheumatic torticollis. The subsequent course served to demonstrate its true syphilitic nature.

Two examinations were made by the *x*-rays, both of which failed to reveal any lesions of the bone tissue.

I have, therefore, regarded the process as being in the nature of a syphilitic periostitis or perispondylitis, with compression of the adjacent nerve roots. The pain on pressure and jarring of the spine, the local tenderness and rigidity, were so characteristic of vertebral disease as to rule out a syphilitic pachymeningitis with root involvement.

CASE II.—Syphilitic periostitis or perispondylitis of the cervical region, with pain and rigidity of the neck, motor and sensory disturbances of the right upper extremity, distinct tenderness and thickening in the lateral region of the cervical column.

History. Patient is an Italian, aged twenty-seven years; a barber by occupation. He was admitted to the New York Hospital, August 14, 1907, where I saw him on several occasions in consultation with Dr. Conner, the attending physician.

Previous History. In 1898 he contracted a venereal ulcer, for which he received only local treatment. No secondaries were noted by the patient. He remained in good general health until March, 1902, when headaches appeared. At first in the left frontal region, later becoming general. They were quite severe, with marked nocturnal exacerbations. He was admitted to the New York Hospital, March 22, 1902. Physical examination is negative, except for a double optic neuritis. The diagnosis of cerebral syphilis was made, and all symptoms cleared up rapidly after a course of mercury and iodides.

On December 1, 1903, he was readmitted to the New York Hospital with headaches of one month's duration, situated chiefly on the right side of the head in the temporal region. The headaches were quite severe. There were distinct nocturnal exacerbations, with tenderness on pressure over the right parietal bone, but no bony nodules could be felt. He also had some pain in the anterior aspect of the left thigh and of the left leg. There was no vertigo, vomiting, or diplopia. The optic disks were normal. The general physical examination was negative, save for some secondary anemia (hemoglobin, 60 per cent.). After a short course of antisiphilitic treatment the symptoms completely disappeared and the patient was discharged. A clinical diagnosis of cerebral syphilis was made.

Present Illness. Patient was re-admitted to the New York Hospital August 14, 1907, with the following history: For the past seven months he has had pains in the back and sides of the neck and in the left shoulder, gradually becoming more severe. For three months he had been unable to work. The left elbow is slightly swollen and tender and is the seat of occasional spontaneous pain. He also has headaches, and because of the nocturnal increase of the pain, sleep has been almost impossible for many weeks. For the past five days, he has had severe pains in the region of the right shoulder, and has developed a weakness, with

paresthesia of the right upper extremity. The neck is also stiff, and the movements are painful. There is no vertigo, vomiting, nor diplopia; no vesical trouble.

Physical Examination. The gait and station are normal, except for an evident stiffness of the neck and fixation of the head. The movements of the neck are restricted in all directions, and cause considerable pain. The cervical spine is quite tender to pressure on both sides, especially on the right. The spinus processes, however, are not tender on percussion. Jarring of the spine causes pain, which is referred to the cervical region. The movements of the dorsal and lumbar spine are free and painless. The pupils are equal and react to light and accommodation. There are no cranial nerve palsies or nystagmus, and the optic disks are normal. There is considerable weakness of the right upper extremity; and especially in the movements of abduction and elevation of the arm. Sensations to touch, pain, and temperature are diminished over the whole of the right upper extremity. There is marked tenderness along the lateral portion of the cervical spine where the nerves emerge from the intervertebral foramen, but especially on the right side. Palpation also shows some general thickening and enlargement in this region of the spine. Both shoulder-joints are freely movable and painless. The left elbow-joint is freely movable, but is slightly swollen and tender. There are no tender spots on the skull. All tendon and skin reflexes are present and normal. There is plantar flexion of the toes on both sides (no Babinski). Examination of the heart, lung, and urine are negative. The blood shows slight secondary anemia (hemoglobin, 84 per cent.). The *x*-ray examination of the cervical spine was entirely negative. The temperature curve showed a slight elevation for the first few days, after which it remained normal. Wassermann reaction was positive.

Subsequent Course. The patient was placed upon antisyphilitic treatment, hypodermics of salicylate of mercury, and ascending doses of potassium iodide. There was a rapid subsidence of all symptoms.

August 27. The pains had diminished, and the movements and sensation of the right upper extremity were normal. Some stiffness of the cervical spine, with pain and tenderness, still persisted.

September 14. Pain had practically disappeared. Can now move the head in all directions, but the movements are still somewhat restricted, and there is still present some lateral thickening in the cervical region, which is tender to pressure.

Patient was referred to the out-patient department for further treatment, and eventually made a complete recovery.

Remarks. The vertebral symptoms in this case had been preceded by two previous attacks, diagnosed as cerebral lues, both of which cleared up completely under antisyphilitic treatment. The verte-

bral symptoms came on gradually, and were of seven months' duration, and were limited to the cervical region. There was in addition to rigidity and pain on jarring in the cervical region, marked tenderness along the lateral aspect of the vertebræ where the nerve roots emerge. This was especially localized upon the right side, where a distinct thickening and enlargement was palpable. The neural symptoms made their appearance about six months after the onset of the vertebral disease, and were evidently of root or plexus origin. They consisted of weakness, with objective sensory disturbances in the right upper extremity. There were no evidences of spinal-cord involvement. All symptoms subsided under specific treatment.

CASE III.—Syphilitic spondylitis of the upper cervical region; sudden onset, with pain and rigidity in August, 1907; improvement under specific treatment; frequent recurrences of pain and stiffness from lack of continuous treatment; in December, 1910, development of acute symptoms with vomiting, vertigo, and headache, followed by numbness and weakness on the right side, and an atrophic paralysis of the left side of the tongue (hemiplegia alternans); improvement under antisyphilitic treatment; in November, 1911, there was still rigidity, with thickening and enlargement in the cervical region, and the residual symptoms of hemiplegia alternans.

History. The patient, a negro, aged thirty-seven years; occupation, bellboy; was admitted to the Vanderbilt Clinic, department of nervous diseases, on November 18, 1911. He is married and has one child, aged six years, living and well. His wife has never miscarried.

Six years ago (1905) he contracted syphilis; no general treatment. In August, 1907, he was seized suddenly with pain in the occipital region and in the nape and sides of the neck, which was followed by rigidity and stiffness of all the movements of the head. At the medical clinic where he applied for treatment the case was first regarded as rheumatic myositis, but because of the previous specific infection, he was later treated with iodide of potassium and mercury. The pain rapidly subsided and the rigidity was greatly diminished. Following this improvement, he failed to return for further treatment, although some stiffness of the neck still persisted, and from time to time he had pain in the cervical region. When the pain was severe, he would return for medicine, and after taking the iodides for a short time, the pain ceasing, he would abandon the treatment. When the pain was severe, the neck seemed to be swollen and slightly enlarged in the painful areas.

In November, 1909, he suddenly developed cerebral symptoms; frequent attacks of vomiting, with headache and vertigo. The vomiting was severe and of the cerebral type, and had persisted for two weeks before he was admitted to Roosevelt Hospital, on November 24, 1909. These general cerebral symptoms were soon

followed by weakness and paresthesia of the right arm and leg and some thickness of speech, due to a paralysis and atrophy of the



FIG. 2.—Case III. Old syphilitic spondylitis of the cervical region, showing rigidity of neck and slight torticollis position of the head.



FIG. 3.—Case III. Syphilitic spondylitis of cervical region, posterior view.

left side of the tongue (hemiplegia alternans). The heart and lungs and urine were reported negative in the hospital history.

The Wassermann reaction was negative on December 17, 1909. There was rigidity, with moderate thickening and tenderness, along the lateral aspect of the cervical region of the spine. The general cerebral symptoms cleared up promptly under antiluetic treatment. The patient was discharged with the symptoms of hemiplegia alternans persisting. There was still some stiffness of the neck and an occasional pain, especially at night.

November 18, 1911. Patient returned to the Vanderbilt Clinic, complaining of pain and stiffness in the cervical region, and was referred to the Neurological Clinic, where he came under my observation.

Physical Examination. The head is in a slightly torticollis position, the chin directed toward the left (see Figs. 2 and 3). All movements—rotation, flexion, and extension—are restricted. Jarring of the spine causes pain in the upper cervical region (first, second, and third cervical). There is some thickening in the region of the lateral processes on both sides of the neck, especially on the right. There is a slight compensatory lateral curvature of the spine. Pupils are equal and react normally. Ocular excursions are normal except for a slight lateral nystagmus. Vision and the sense of smell are normal, as are the fifth and seventh nerves. There is diminished hearing on the right side (central deafness). The soft palate is equally enervated on the two sides. The tongue deviates sharply toward the left. There is a very pronounced atrophy, with deep furrows and marked fibrillation of the left side of the tongue. There is also some atrophy, with fibrillary twitchings on the right side as well, but to a lesser degree. There is no difficulty in deglutition, and the voice is normal. No laryngoscopic examination. The sternocleidomastoid and trapezius are normal on the two sides. The right arm and leg show some weakness, more especially the leg. The tendon reflexes of the right lower extremity are exaggerated, and there is ankle-clonus. No patellar clonus. The plantar reflex on the right side is diminished, and is of the flexor type. It is normal on left. The abdominal and cremasteric reflexes are diminished on the right side. The superficial sensibility is lost over the right lower extremity and over the lower half of the right side of the trunk; above this the sensibility is simply diminished. The sensibility of the face is normal. The deep sensibility of the upper and lower extremities is normal.

The man was placed upon anti-syphilitic treatment and the pain and stiffness in the neck rapidly improved. As was always the case in this particular patient, as soon as the pain ceased he lost interest in the treatment and ceased to continue it. There is, however, no question as to the rapid response at all times to anti-syphilitic treatment, especially the iodides.

An x-ray examination at the Roosevelt Hospital showed thicken-

ing and enlargement of the bodies of the third, fourth, and fifth cervical vertebræ, as well as of certain of the lateral processes, especially on the right side. There were no evidences of destruction or cavity formation of the vertebræ or intervertebral disks.

REMARKS. The syphilitic spondylitis in this case had run a very gradual course, extending over a period of four years. The chronicity of the symptoms and the permanency of the rigidity may be referred to the intermittent and incomplete manner in which the antisyphilitic treatment was carried out. This never failed, however, to produce subsidence of pain and diminution of rigidity.

An interesting and unusual feature is the occurrence of hemiplegia alternans, a unilateral atrophic paralysis of the tongue with contralateral hemiplegia, due to a lesion in the lower portion of the medulla oblongata on the left side. It is possible that this lesion of the medulla may have been caused by syphilitic disease of the vertebral artery as it coursed through the transverse process. Cerebral lues independent of the vertebral disease cannot, however, be excluded.

CASE IV.—*Syphilitic osteitis of the lower lumbar vertebra and sacrum, with gummatous infiltrations of the cauda equina, followed by paralysis and sensory disturbances, in the distribution of both sciatic nerves, and accompanied by marked rigidity, deformity, and tenderness of the lumbosacral spine; autopsy revealed syphilitic osteitis of the lower lumbar vertebra and sacrum, with multiple gummata of the cauda equina.*

History. Patient, a man, aged fifty-three years, was admitted to the Montefiore Home for Chronic Invalids, January 5, 1896. He denies all venereal disease, and enjoyed excellent health up to one year ago, when he developed pains in the distribution of the right sciatic nerve, which were especially severe at night. There was some tingling and numbness on the outer side of the right leg. A little later similar pains and paresthesia developed in the same distribution on the left side. He also had severe pain in the lower portion of the back over the sacrolumbar region, especially in the sitting posture, so that he was obliged to use a cushion to protect this region from pressure. Pain was particularly severe in the sitting or recumbent posture, and he would experience a little relief in standing and in walking. The pain became gradually more severe, and he was obliged to resort to narcotics and analgesics for relief.

On October 7, 1895, he was admitted to Mt. Sinai Hospital, and while there developed extensive paralyses of the lower extremities, with incontinence of urine and feces.

On his admission to the Montefiore Home, he complained of shooting pains in both lower extremities and severe pain in the lower portion of the spine, especially in the sitting and recumbent posture; incontinence of urine and feces and impotency.

Status Præsens (Dr. Joseph Fraenkel). Patient is unable to walk because of weakness in the lower extremities. On attempting to stand he complains of pain in the lower portion of the spine, and sudden pains in the feet and legs. There is a constant dribbling of urine. Pupils are small and equal; reaction to light slight; reactions on accommodation are present. Ocular excursions are normal. Motility, coördination, muscle volume, and sensibility of the upper extremities are normal. There is a well-marked kyphoscoliosis at the junction of the dorsolumbar region, the scoliosis being the more marked deformity. The spine is tender on pressure, beginning at the first dorsal vertebra and extending to the coccyx. This sensitiveness is especially marked over the eleventh and twelfth dorsal and the first lumbar vertebra and over the lower portion of the sacrum. It is acute on percussion. Over the lower portion of the sacrum there is a slight tumefaction. The movements of the column show great rigidity, and are accompanied by considerable pain. There is no visible atrophy nor fibrillation of the muscles of the back. There is some weakness of the abdominal muscles in their lower portion. Both lower extremities are paretic, more especially the left. The calves of both legs are markedly atrophic. The knee-jerk is lively on the right side, with patellar clonus; absent on the left. Both ankle-jerks are absent. The abdominal, cremaster, and plantar reflexes are absent on both sides.

Sensation. There is tactile and thermal anesthesia in the distribution of both sciatic nerves. Sensibility to pain is diminished in the same area. There is also anesthesia of the left buttock, left side of the scrotum, and penis and perianal region. The deep sensibility of the toes is disturbed. Heart and lungs are normal.

Death occurred February 28, 1896. Postmortem examination showed extensive syphilitic osteitis of the lower lumbar vertebra and the upper portion of the sacrum. There was a good-sized erosion of the first sacral segment. The strands of the cauda equina were matted together by extensive syphilitic infiltrations, and contained four gummata the size of hazelnuts. The histological examination of sacral segment and cauda equina present the typical lesions of syphilis.

REMARKS. This case is interesting because of its unusual localization, syphilis of the lumbar region being the rarest of all types. Cases of syphilitic caries of the sacrum have been described by Yvaren and by Westphal. In Westphal's case it was associated with typical sacral anesthesia.

CONCLUDING REMARKS. Syphilitic spondylitis and perispondylitis while rare are nevertheless sufficiently frequent to be given careful consideration in every case of acute or chronic vertebral disease. The onset may be sudden, simulating an acute rheumatic affection, or it may develop gradually and run an exceedingly chronic and protracted course.

Localization in the cervical region, especially, should awaken the

suspicion of lues, as more than half of the recorded cases are of this region. It may, however, occur in any portion of the spinal column.

Of 100 cases available for analysis, I found that 25 per cent. were associated with some complication referable to the nervous system. These were either of the nerve roots and plexus or of the spinal cord itself.

Generally speaking, in this group of cases with neural complications, the symptoms indicated a lesion of the spinal cord in two-thirds; in the remaining third, the neural symptoms were limited to an involvement of the nerve roots or plexus.

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SYPHILIS OF THE ESOPHAGUS.

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It is a well-established clinical fact that in a given individual, certain of the systems seem more predisposed in their susceptibility to the *Spirocheta pallida* than do others. The peculiar predisposition for the exclusive localization in the nervous system, for example, occurs in those cases in which the mucocutaneous system is relatively uninvolved, and, conversely, where the mucocutaneous system is early involved with severe manifestations it is exceptional to find late nervous sequelæ. To what extent this susceptibility is due to the virulence or strain of the organism, on the one hand, or to the individual lowered resistance of the affected system, on the other, is as yet undetermined.

The high susceptibility of the mouth and pharynx in early syphilis and the not infrequent occurrence of syphilitic manifestations in the rectum late in the disease make the apparent immunity of the rest of the digestive system a rather striking feature. Leaving out the mouth and rectum the digestive tube seems to enjoy an immunity to the action of the syphilitic organism which is without parallel in any other system. Syphilis of the esophagus, of the stomach, and small intestine is of exceedingly rare occurrence. Indeed its occurrence was denied in many of the earlier works on pathology, surgery, and medicine.

The first mention of syphilis of the esophagus is found in the writings of Severinus¹ in the middle of the eighteenth century. Gastou,² who wrote the chapter on syphilis of the gastro-intestinal system in Fournier's monumental work, has been able to collect 40 cases of esophageal syphilis. In 13 of these cases the diagnosis could be verified at autopsy; 6 cases improved under the influence of antisiphilitic treatment and did not come to autopsy; in 11 cases there was dysphagia, with the signs of stricture, and 10 cases of the 40 Gastou holds open to doubt as to the correctness of the diagnosis.

Dysphagia, leading to marasmus and death, in the course of syphilis is mentioned by Jean Astruc³ (1736) and also by Carmichael⁴ (1815). Ruysch⁵ (1717) and Haller⁶ (1768) report cases in which apparently syphilitic stenosis of the esophagus was cured

¹ Cited by Lublinski, 1580-1636 (Berl. klin. Woch., 1883, pp. 499 and 515).

² *Traite de la Syphilis*, A Fournier, 1906, ii, 465.

³ *De Morbis venereis libri sex*, Paris, 1736.

⁴ *An Essay on Venereal Diseases*, Dublin, 1815, p. 270.

⁵ *Adv. anatomico medica chirurgica*, Amsterdam, 1717-1723. (Cited by Lublinski.)

⁶ *Opuscula pathologica*, etc., Laus, 1768. (Cited by Lublinski.)

by mercurial treatment. The anatomy of esophageal syphilis was first described by Lieutaud.⁷ Notwithstanding these early reports of esophageal syphilis, many of the earlier texts on pathology and surgery failed to give a place to syphilis of the esophagus. In Bardeleben's⁸ text, however, also in Strümpell's,⁹ ulcerations of the esophagus due to syphilis are described. Koenig,¹⁰ writing in Billroth's *System*, also gives mention to esophageal syphilis. The subject receives considerable mention in *Virchow's Archiv* by Virchow¹¹ himself. Herein are included the autopsy report and the full anatomical description of esophageal stenosis in syphilis and of esophageal ulcerating gumma.

In 1863 Wilks¹² showed a specimen from the museum of Guy's Hospital which showed sclerosis of the upper portion of the esophagus following syphilitic ulceration. The same observation is recorded in 1875 by Klob.¹³ The first, however, to call attention to esophageal syphilis in an excellent monograph was James West¹⁴ (1860). This author collected from his vast experience three cases of syphilis of the esophagus, in two of which he was able to corroborate his clinical findings at autopsy. The other case improved on treatment and remained well. West cites also in his paper cases by Langston-Parker¹⁵ and Clapton,¹⁶ which by analysis could be nothing but cases of syphilitic esophagitis.

Follin,¹⁷ in 1861, records a case of dysphagia of undoubted syphilitic nature. Robert,¹⁸ in 1861, cited by Lubinski, in discussing dysphagia in syphilis, avers that the autopsy findings in such cases show at times lesions in the pharynx, in the larynx, and in the esophagus. Morrell MacKenzie,¹⁹ in 1874, reports a case of esophageal stenosis at the level of the sixth dorsal vertebra in an old syphilitic which yielded in a short time to antisymphilitic medication. A most excellent treatise on the subject is published in 1883 by Lubinski,²⁰ who has cited literature at great length and added two observations of his own. Both these cases recovered completely, but there could be no doubt from the excellent description and history that these were examples of true syphilitic esophagitis.

⁷ *Historia anatomico medica sistens numerosissima cadaverum humanorum exstirpitia*, Paris, 1767.

⁸ *Lehrbuch der Chirurgie und Operationslehre*, 8th edition, iii, 543.

⁹ *Lehrbuch der speciellen Pathologie u. Therapie inneren Krankheiten*, 1912, 18th edition, i, 518.

¹⁰ *Handbuch der allgemeine u. specielle Chirurgie*, Pitha u. Billroth, 1880, iii, 17-18.

¹¹ *Archiv f. pathologische Anatomie u. Physiologie*, 1856, xv, 217-315.

¹² *On the Syphilitic Affections of the Internal Organs*, London, 1863, p. 41.

¹³ *Wien. med. Woch.*, 1875, xxv, 210.

¹⁴ *Dublin Quart. Jour. Med. Sci.*, 1860, xxx, 29; *ibid.*, *Lancet*, 1872, ii, 291.

¹⁵ *Lancet*, 1872, ii, 292.

¹⁶ *St. Thomas' Hosp. Rep.*, 1871, new series, ii, 177.

¹⁷ *Traite Élémentaire*, Paris, 1861, i, 696.

¹⁸ *Nouveau Traite des maladies veneriennes*, Paris, 1861.

¹⁹ *Lancet*, 1874, i, 754.

²⁰ *Berl. klin. Woch.*, 1883, pp. 499 and 515.

In 1887 a typical case is described by Potain.²¹ According to Gastou,²² gastrotomy is reported for syphilitic stenosis in 1870 by Maury. In 1884 Jullien²³ published a monograph on esophageal syphilis based on nineteen authentic cases which he had collected. In the American literature a single case, according to other authors, is reported by Godon in 1880. I have been unable, however, to verify this observation, as the reference is evidently misquoted as to the date.

Apparent paralysis of the muscularis of the esophagus due to syphilis is described by Saundby²⁴ in recent literature. In the case described by this author and in another cited by him and described by Mott²⁵ there was sudden paralysis of the esophagus, as shown by dysphagia, without any stenosis, occurring in syphilitic individuals. In both cases there was evidently central nervous syphilis antedating the esophageal symptoms, and both cases responded well to antisymphilitic treatment. Strictly speaking, these cases would hardly be classed as disease of the esophagus itself, but have rather to do with the involvement of its innervation, directly referable to syphilitic disease of the central nervous system.

Careful study of the cases described and the one observation of my own which is to follow, reveal no single etiological factor for the occurrence of the lesions in the esophagus. The lesions occurred somewhat more often in men than in women, although it is a striking fact that all of West's cases occurred in females. In no case did injury seem to play any role. Of striking significance, however, is the fact that in a large number of cases there were lesions in the mouth and pharynx, suggesting either the continuity of the infection, or speaking more directly for the localization of the process in the digestive system. It is also a striking fact that many of the earlier cases were evidently fulminating in type with rupia and extensive caries. Such are the cases described by Wilks, Carmichael, and West.

The pathology of syphilitic esophagitis depends upon the time at which the case may be studied. Secondary superficial erosions and ulcerations, such as occur in the mouth and pharynx are not described in the esophagus. Such cases do not come to autopsy frequently. The not infrequent dysphagia, however, that occurs in secondary syphilis could, I think, well be due to superficial erosive syphilides. The great bulk of our cases, however, are those of tertiary syphilis. Here it would seem that the process is usually a gummatous condition of the submucosa which undergoes one of

²¹ Gazette Médicale de Paris, 1887, iv, 193; *ibid.*, La Semaine Médicale, 7, 1887; vii, 261.

²² *Loc. cit.*

²³ British Med. Jour., January 31, 1914, No. 2770, p. 239.

²⁴ A System of Syphilis, Power and Murphy, iv, 92.

²⁵ *Loc. cit.*

two changes. It may, under appropriate treatment, or even spontaneously, involute by fatty degeneration, such as is described by Lublinski and by West, the second case of Follin's, and in the case cited by West of Clapton's. In the event, however, of no treatment, or occasionally in spite of treatment, such gummatous changes are likely to undergo early ulceration. If these heal, there results a scar with a marked tendency to contraction and resulting stenosis. Finally, there may be, instead of localized scarring and contraction, a diffuse process encircling the entire tube for the greater part of its length and causing almost complete stenosis and impassibility for all solid food. This last condition is accurately described in the first of the Virchow cases and in the case described by Wilks.

To these cases we should like to append one which we have had the opportunity of observing at the University Hospital during the past year. The patient, a woman, aged forty years, was transferred to my department by my colleague, Dr. Canfield, of the Otolaryngological service. She was admitted to the hospital for throat trouble December 18, 1913. Her family history was of no importance save that the patient had had two miscarriages following two healthy pregnancies. Nine years previous to her admission she had ulcers on the left cornea, and finally the eye was removed. Eight or nine years ago the patient began to experience a little difficulty in swallowing. This did not become severe, however, until six years ago, when she would occasionally become choked on eating. There was also considerable pain at this time during the act of deglutition, and soreness of the mouth was noticed on taking of hot or sour food. At this time the glands of the neck were also considerably enlarged.

Status Præsens.—The patient is an extremely anemic, rather cachetic woman. The left eye is glass. The right pupil reacts to light and in accommodation, but shows some interstitial keratitis. The skin of the body is entirely clean except for a few pigmented macules about the hips, knees, and back. The tongue is absolutely smooth and devoid of papillæ. The mouth is dry and there is extensive sclerosis of the entire buccal cavity. The entire mucous membrane of the mouth and tongue give the appearance almost of a kraurosis. There is no general adenopathy. The liver and spleen are not palpable. The urine and blood are normal. An x-ray plate of the patient's chest shows a periostitis about the middle of the left humerus. The occurrence of the esophageal lesion was accidentally discovered, as the patient did not complain of distinctly painful deglutition. On December 29 a small morsel of food became impacted in the esophagus and remained there one hour and twenty minutes in spite of efforts to dislodge it. At this time a small caliber stomach-tube was passed in order to relieve the patient of her dysphagia, and it was found that this could not

be passed into the esophagus at all on account of the very evident constriction just below the larynx. On December 30 an esophagoscopy was performed upon the patient by Dr. Canfield, and it was discovered that there was a marked sclerosis of the entire tube. Nothing but the smallest sized filiform bougie could be passed into the esophagus and down to the stomach. On January 17 the patient was given a bismuth paste and fluoroscoped. During the act of deglutition a definite stricture was noted just below the level of the lower portion of the larynx, and a second stricture just above the cardia. In both cases there was a distinct pouch found above the point of stricture and the bismuth could be seen passing very slowly through the constricted portions. An x-ray photograph was attempted and shows fairly well the uppermost of the two strictures. The patient was placed upon a combined salvarsan and mercurial therapy and her condition improved markedly. An attempt was also made to dilate the strictures with bougies of increasing size, and following each application deglutition was somewhat easier. At the present time the patient is receiving vigorous mercurialization and tri-weekly esophageal dilatation.

The symptoms of syphilitic esophagitis do not differ materially from the symptoms due to other forms of esophageal disease. Of first rank in importance is difficulty in deglutition. This, as a rule, is a gradual process. The patient notices at first slight difficulty in swallowing solid food. Then he can swallow solid food only in small morsels, and later solid food becomes impossible to swallow; it is regurgitated and liquid food only can pass into the stomach. In time this too becomes difficult, so that in rare cases there is complete stenosis. Pain is not a marked symptom, except during the act of swallowing. Where there is ulceration, pain may be present in repose as well as during deglutition. In old-standing cases where scarring and consequent narrowing of the tube occur the pain during attempted swallowing may be very severe.

Anemia, weakness, denutrition, and later cachexia are frequent late in the disease. These may find their cause either in coincident syphilis of other parts which is likely to approach a malignant type or, in cases in which an esophageal lesion is present without other manifestations of active syphilis, the above symptoms are readily explained on the ground of actual starvation.

The differential diagnosis is at times extremely difficult. In the absence of other manifestations of syphilis, carcinoma, compression of the esophagus by mediastinal tumors, and spastic stenosis are the conditions which are most readily confounded with the condition in question. The marked cachexia which may accompany the condition late, renders its differential diagnosis from carcinoma the more difficult. In general the carcinoma is apt to be more painful and appears more frequently in the lower part of the

esophagus than in the upper. Emesis and hematemesis are more common in carcinoma than in syphilis. The Wassermann reaction is of course a most valuable guide in the differential diagnosis. It must be remembered, however, that carcinoma could quite possibly find a starting place in an old gumma, so that a positive Wassermann, while presumptive evidence of the syphilitic nature of the process, would not of necessity rule out carcinoma. A valuable aid in the diagnosis as well as to the localization of the lesions lies in the *x-ray* and fluoroscopic examination. In the case described by myself the confirmation of the diagnosis was most satisfactorily established by this means. It was noted in the fluoroscope that bismuth taken a half-hour previously was



x-ray photograph showing the uppermost of the two strictures.

retained in two large pouches situated just above extensive areas of stricture. In the one case, as may be seen by the radiograph, the pouch is located just below the larynx. Just below this point the canal seems obliterated. The second pouch is noted about 6 cm. above the cardia, and from this point to the stomach the canal is again obliterated. This picture could obviously not be produced by carcinoma; that is, two extensive foci of disease separated by a relatively normal portion of the tube. The fluoroscope and radiograph would also serve obviously to distinguish such cases from those of simple spasm. The absence of shadows in the mediastinum and the absence of physical signs by percussion

readily differentiate the condition from mediastinal growths giving rise to esophageal compression.

The prognosis of the condition seems to depend entirely upon the time at which the condition is recognized. In those cases in which there is gummatous infiltration with a low grade of stenosis the prognosis under antisyphilitic is excellent. Where the gumma is ulcerated the prognosis is more grave, because it is sure to be followed by more or less constriction following the healing of such ulceration. In those cases in which there is extensive fibrosis of long standing the prognosis is exceedingly grave, and for the most part these patients die of marasmus.

The treatment of the condition must be a most energetic one. Up to the present time mercury and iodide have been of service in those cases in which a good prognosis could be looked for. In any event the esophagus should be carefully sounded following the antisyphilitic treatment, and the contraction, if there be one, should be gradually dilated much in the same way as in the treatment of urethral stricture. In my own case I may say that the patient improved markedly under the combined salvarsan and mercurial therapy, notwithstanding the fact that she belonged to the worst class of cases—namely, that in which there is complete fibrosis of the canal. The esophagus now admits a No. 11 bougie, the patient has taken on weight, eats solid food with greater ease, and is in a fair way toward partial recovery.

In conclusion I venture to express the opinion that syphilitic esophagitis, though a rare condition, is nevertheless not so infrequent as the rather scanty literature on the subject would seem to indicate. It is not improbable that many cases which die in cachexia supposedly with carcinoma of the esophagus are cases of death from marasmus as the result of syphilitic esophagitis. The same relation that Billroth showed between gumma and carcinoma of the tongue without doubt also exists in the esophagus. In these days of refined laboratory technique, however, mistakes in diagnosis are less apt to occur. It goes without saying that any case of esophageal stricture or esophageal tumor should not escape a most careful scrutiny, with a view to its possible syphilitic nature.

SCHISTOSOMIASIS JAPONICA: A CLINICAL AND PATHOLOGICAL STUDY OF TWO CASES.

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To students of medicine in the temperate zones the swiftly advancing knowledge of the diseases peculiar to the tropics presented in such a work as Manson's *Tropical Diseases* has been more or less startling in its revelation of the widespread prevalence of diseases unknown in these parts, unique in etiology, and presenting entirely new problems in prophylaxis and treatment. So far as the etiology of these diseases has been revealed, it has been found to turn upon the activities of parasites, either bacteria or more highly developed organisms. So true is this that parasites come to occupy the mind of the student of tropical diseases, and we find Manson writing that "nearly all diseases, directly or indirectly, are caused by germs." The life-history of many of these parasites is most involved, and consequently the prevention and treatment of the resulting diseases present problems of great difficulty and interest. The constantly increasing movement of people from one part of the earth to the other carries with it the possibility that individuals suffering from some of the rarest of these so-called tropical diseases may be met with in this country, and a knowledge of these diseases may therefore become of importance to any physician.

It should also be said that the presence of infected individuals in this country renders it possible that parasites or germs heretofore limited to tropical distribution may be spread broadly here, and render endemic diseases heretofore unknown. Fortunately, however, the spread of these parasites seems to demand tropical conditions, or the presence of intermediary hosts peculiar to the tropics, so that thus far our knowledge of them has been limited to imported cases, such as the following:

CASE I.—K. O., aged twenty-eight years; male; Japanese. Admitted to medical service of Presbyterian Hospital, November 21, 1910.

Family and personal history are negative.

Previous Illnesses. He has always been healthy except for some trouble with knees attributed by patient to beriberi, which lasted only one week. Five years ago he was in Bellevue Hospital seven weeks with a fever, the nature of which was not discovered. Since then he has been perfectly well.

Present Illness. He was perfectly well until the evening before admission, when about one hour after supper he began to feel queer and had a burning sensation in the stomach. At 9 P.M. he vomited. The vomitus consisted of the food eaten, mixed with some dark blood. He vomited again a little later, and still a third time; in each instance the vomitus contained dark blood. Aside from a queer feeling in the stomach and some burning in the upper abdomen, patient had no other symptoms. He slept, though not soundly, and this morning after taking some orange juice he vomited again one hour later, and still again about 10 A.M. Each time there was blood in the vomitus. No blood was ever noticed in the stools.

Physical Examination. Patient is markedly pale; mentally clear; well nourished. Breathing somewhat increased in rate. The skin, conjunctivæ, and mucous membranes are pale.

Heart: Normal size and position. Action is regular but quite rapid. Sounds are of fair quality; there is a faint systolic murmur at apex. Pulses are equal, regular, small, and soft. Rate 116.

Lungs: Normal.

Liver: Upper border; flatness is at seventh rib. Edge is not felt. Percussion is obscured by epigastric dullness and abdominal tympany.

Spleen: Enlarged to a point about two inches below the costal margin.

Abdomen: Rather full and hypertympanitic, with some abnormal dullness in epigastrium. Over the epigastrium there is some general tenderness. Otherwise the examination is entirely negative.

November 21. Urine: 1030; acid; very faint trace of albumin; a few leukocytes and epithelial cells.

November 21. Blood: Hemoglobin, 80 per cent.; white blood cells, 9100; polynuclears, 85 per cent.; lymphocytes, 12 per cent.; transitionals, 2.5 per cent.; basophiles, 0.5 per cent.

November 22. Hemoglobin, 68 per cent.

November 22. At 4.45 P.M. yesterday patient suddenly vomited a quantity of blood estimated at twelve ounces. An injection of morphine was immediately given. Again at 9.15 P.M. he vomited ten ounces of blood. An ice coil was applied to the abdomen and he slept quietly until 3.30 A.M., when he again vomited ten ounces. At 4 A.M., eight ounces, and again at 10.30 A.M., eight ounces of blood were vomited. After 11.30 A.M. he failed rapidly, and died at noon before an infusion could be given. An interesting feature was the fact that the spleen, quite large yesterday on admission, was much reduced in size this morning.

Autopsy, November 23 (by Dr. Cecil), twenty-five hours after death. The body is that of a young Jap measuring 150 cm. in length. Postmortem rigidity is present. Rigor mortis in dependent parts. Pupils are equal and moderately dilated.

On opening the abdomen the peritoneal surfaces are smooth

and glistening. There are a few adhesions about the appendix, and the neighboring fat contains considerable dense fibrous tissue.

The pericardial sac is normal.

The heart weighs 280 grams. The epicardium is smooth and glistening. The tricuspid and pulmonary valves are normal. The mitral valve is normal. The aortic leaflets are slightly thickened. There are few plaques of atheroma at the base of the aorta. The left ventricular wall measures 13 to 15 mm. in thickness. The myocardium is dark brown in color. The coronary arteries are normal.

The right lung weighs 330 grams. It lies free in the pleural cavity. Its surface is translucent and glistening. The tissue is everywhere crepitant. The cut surface is pale. The structures at the hilum are normal.



FIG. 1.—Liver from Case I, showing marked cirrhosis and fibrous adhesions on surface.

The left lung is collapsed and is everywhere adherent to the thoracic wall and the diaphragm. The pleural covering of the lung is considerably thickened, especially along the posterior border, where it forms a dense, thick, white membrane. The left lung weighs 320 grams, with diaphragm attached. The tissue is resilient and contains very little air. The cut surface is dark red and hemorrhagic. The structures at the hilum are normal.

The spleen is greatly enlarged. It weighs 900 grams. It measures 22 x 15 x 8 cm. The surface of the spleen is pinkish red, smooth and glistening. The organ has a peculiar leathery consistence. Cut surface is pinkish red and oozes very little pulp. The Mal-

pligian bodies and trabeculae are prominent. The splenic artery and vein are free from thrombi.

The liver (Fig. 1) weighs 400 grams. It is somewhat smaller than the normal, and very firm. The surface has a light grayish-brown color, and is coarsely granular, being traversed by irregular fissures of various depths. On the inferior surface of the liver the fissures are deeper than elsewhere, and divide the surface into a large number of nodules, varying from 0.1 to 2 cm. in diameter. Cut surface of the liver is light brown, opaque, and hob-nailed. The normal lobulation has been replaced by lobules of various sizes separated by translucent bands. The gall-bladder contains dark-brown viscid bile. The bile ducts are patent. There is no thrombosis of the portal vessels.

The pancreas is pale and firm. On section the lobules are easily separated. A few islands are visible. The pancreatic duct is patent. The lymph nodes surrounding the pancreas are enlarged.

The left kidney weighs 120 grams. The capsule strips easily, exposing a smooth pale surface. On section the cortical markings are distinctly seen, and pyramids are sharply defined.

The right kidney weighs 110 grams. It is similar to the left kidney in all respects. Pelves and ureters are normal. The suprarenal glands are normal. The bladder is normal.

The rectum contains dark, black, tarry material, evidently old blood. There are a few small dark-red irregularities on the mucosa, which have the appearance of partially healed ulcers.

The mesenteric lymph nodes are slightly enlarged.

The aorta is elastic, and there are a few plaques of atheroma.

The esophagus shows a few dilated veins.

The stomach is moderately dilated and contains dark-red fluid blood.

The gastric mucosa is dark red and glistening and mottled with small dark spots in many points. At no point, however, is there any visible break in the mucosa.

Duodenum contains dark brownish material. Jejunum and ileum contain dark-red coagulated blood. The mucosa of the small intestine is everywhere smooth and pale. The solitary follicles in the small gut are prominent. Attached to the head of the cecum there is some dense scar tissue which on section presents the appearance of a healed focus of some kind. Just below the ileocecal valve there are several small dark red projections on the surface of the mucosa which have the appearance of polyps. The large intestine is filled with black, tarry material. Except for the polyp-like structures, the mucosa of the large intestine is smooth and glistening.

Microscopic Examination. Spleen: There is considerable increase of interstitial tissue in both sinuses and follicles. The trabeculae are much thickened and in places hyaline. In the interstices of the connective-tissue red-blood cells and leukocytes, chiefly of

lymphoid variety, occur in considerable numbers. The walls of the bloodvessels are much thickened, and there is considerable hyaline degeneration of the dense fibrous tissue around them. In many places red-blood cells show signs of disintegration.

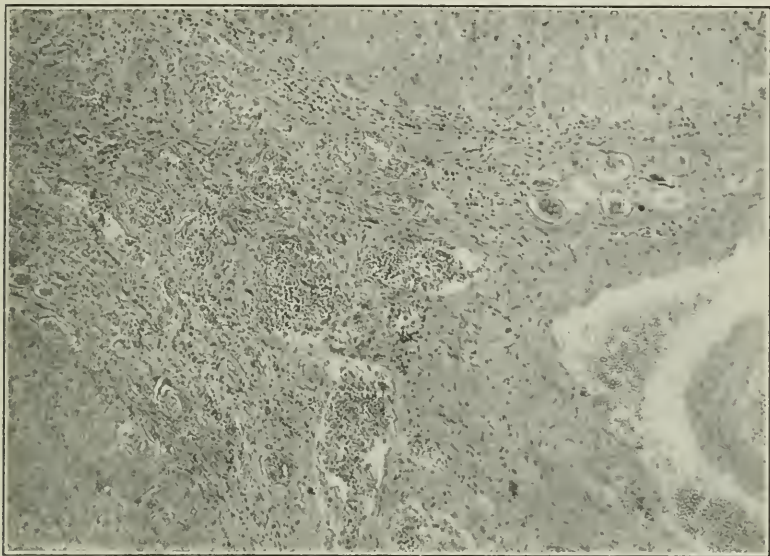


FIG. 2.—Section of liver from Case I. (About 300 \times .) Marked intralobular proliferation of fibrous tissue with infiltration of lymphoid cells. At several points can be seen the ova of *Schistosomum japonicum*, some of them disintegrating.

Liver: There is a well-marked increase of connective tissue between the lobules (Fig. 2), especially along the courses of the portal vessels. The new-formed tissue is dense and infiltrated, with considerable numbers of lymphoid cells. There is some regeneration of small bile ducts. At many points in the interstices of the stroma there can be seen one or several sharply defined ova of some parasite; they are oval shaped and surrounded by thin refractile membranes, which may in turn be enclosed by foreign-body giant cells. A few of the ova have penetrated into the lobules, but the greater number lie in the interlobular tissue. Most of the ova are well preserved, and show extensive segmentation. A few, however, have been compressed and more are disintegrated by the fibrous tissue. One ovum is found completely surrounded by a calcareous capsule. The smaller arteries throughout the stroma show considerable thickening of the intimal coat. Except for some compression atrophy, the parenchymatous cells have not suffered.

Pancreas: There is no increase in the interstitial tissue. Islands of Langerhans are rather scarce.

Heart muscle is normal.

Kidneys: Normal, except for a slight thickening of some of the glomerular capsules.

Suprarenal glands: Medulla shows postmortem degeneration. The cortex is normal.

Lungs: The interalveolar septa are congested. Pleura is greatly thickened and hyaline.

Mesenteric lymph node: The follicles are swollen. Here and there in the sinuses occur ova, usually single, and often surrounded by a crescent-shaped giant cell.

Stomach: Mucosa intact. Muscularis and serosa normal.

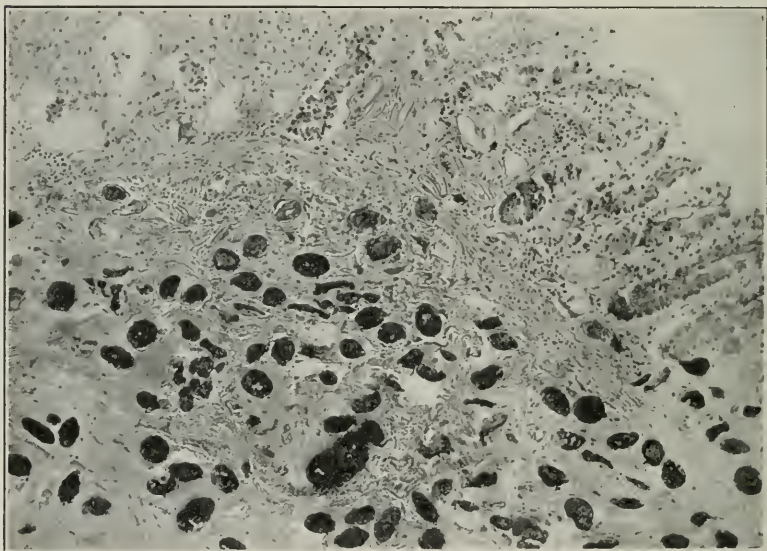


FIG. 3.—Section of ileum from Case I. At several points in the mucosa there are shells of disintegrating ova. In the submucosa many calcified ova and some hyaline degeneration of the stroma.

Ileum: The mucosa is partially autolyzed. At various points in the mucosa and submucosa occur singly or in small groups the ova of some parasite (Fig. 3), similar in shape and general appearance to those observed in the liver. Many of them take a diffuse, deep violet stain with hematoxylin and eosin, as though undergoing calcareous changes. Others appear normal and show segmentation. Still others are shrunken and granular, with wrinkled collapsed capsules. The stroma about the ova shows no change except at one point where there is a cluster of radiating epithelioid cells suggestive of a miliary tubercle.

Appendix: Normal.

Cecum: The mucosa is intact. Section through the polyp shows it to be composed of long papillae covered with hypertrophied

columnar epithelium. The crypts are filled with mucus. The mucosa and submucosa are everywhere infiltrated with ova similar to those found in the ileum. The muscularis contains considerable numbers of leukocytes, especially about the bloodvessels. The serosa is thickened and dense.

Rectum: Section through one of the small red areas shows the following: The mucosa is intact. In the submucosa there is a large collection of ova similar to those described in the cecum and ileum. They are separated from one another by dense connective tissue which shows little or no infiltration. Segmentation has occurred in some of the ova. Small groups of the ova are seen here and there in the muscularis and serosa.

Anatomical Diagnosis. Schistosomiasis japonica, ova of Schistosomum japonicum in intestinal mucosa, liver, and mesenteric lymph glands; interlobular cirrhosis of liver; chronic interstitial splenitis; chronic splenic tumor; hemorrhages into gastro-intestinal tract; chronic fibrous pleuritis; atelectasis of left lung; chronic perityphlitis; papillomata in cecum.

In view of the profuse gastric hemorrhages in this case, the negative findings of the autopsy so far as the stomach was concerned were somewhat surprising. There were certainly no gross ulcerations. The petechiae observed were minute. There was no marked dilatation of the gastric veins suggesting portal obstruction, nor such as is sometimes seen in splenic anemia. Nevertheless, the clinical history and the distribution of the blood at autopsy both indicated that the hemorrhage had come from the stomach. While it has been known that hematemesis may occur purely from diapedesis following congestion of the gastric mucosa, the loss of such large quantities of blood as occurred in this patient without sufficient anatomical lesions of the stomach or duodenum to explain it is, to say the least, unusual. It is quite possible that the profuse hemorrhage, just as it markedly reduced the size of the spleen, may have relieved an enlargement of the gastric veins present during life.

At present we have no knowledge which would justify the correlation of the gastric hemorrhage and the parasitic infection. Tsuchiya¹ has shown that in an apparently sound gastric mucosa the eggs may be found in small numbers, but that usually round-celled infiltration and finally erosion of the mucosa takes place about them. Similar ulceration of the intestinal mucosa accounts for the bloody diarrhea so frequently observed in this disease. While lesions would explain the symptoms of our patient, we were unable to demonstrate ulceration of any kind in the stomach. The hepatic cirrhosis with the presence of ova in the liver has been noted, but there was no evidence of portal obstruction or throm-

¹ Virchow's Arch., 1908, xciii, 323.

bosis. It is well-known that certain parasites secrete hemolytic substances and thus produce anemia, and that hematemesis may occur in any profound anemia. But certainly when the patient was first seen there was no degree of anemia sufficient to warrant such an interpretation of the symptoms. That toxins derived either from the parasites or their ova may directly excite such hemorrhages suggests itself, but such an explanation at present is purely hypothetical.

CASE II.—C. H., aged fifteen years, American, born in Japan; school-boy; admitted to hospital December 10, 1912, complaining of attacks of diarrhea, with bloody, mucous stools.

Previous Illnesses. None, except for one attack of pleurisy.

Present Illness. Five years ago the patient, who had been living in America for four years, went to China, arriving there in February. The following July he was taken acutely ill with chills and high fever. In a day or so large white blotches about one-eighth inch in diameter appeared over the abdomen, chest, and thighs, but none on the exposed body surface. They did not itch and were not painful or tender to touch. In about two weeks they disappeared. The diagnosis of the local physician was angioneurotic edema. The patient's fever, however, continued high in the evening and low or absent in the morning. There was moderate diarrhea, with more or less blood in the stools. The physician finally diagnosed the condition as typhoid fever. He was in bed six weeks and slight fever continued after he was up. During the winter the patient was much better, but had occasional attacks of diarrhea, with bloody stools. No vomiting at any time. The following spring he had a severe attack of diarrhea, with much blood in the stools, this attack lasting for six weeks. In July, 1908, he had chills and fever again for three weeks, with the same bloody diarrhea. He was treated for malaria and also for the diarrhea, which persisted. During the entire following winter, at intervals of five or six weeks, he would have a hard chill followed by profuse sweats and high fever, and shortly after the chill the diarrhea would begin. The patient would go to bed for a day or so. Diarrhea would continue for three or four days and sometimes a week. There was no headache or pain with any of his attacks, except for slight cramps and griping pain in the bowels before a movement. The next spring the patient went swimming and waded much in stagnant ponds. One morning after he had been wading in the water for several hours, a profuse rash appeared on both legs from his knees to the ankles. The rash was in the form of bright-red pimples, about the size of a black-headed pin. The next morning the rash had disappeared. The following afternoon the patient was taken acutely ill with a hard chill, burning fever, and severe abdominal pain in the region of the appendix. Considerable abdominal distention and rigidity were present. Vomiting was so severe that he could

not retain water. There were frequent stools, composed chiefly of blood and mucus. On the following day the pain shifted to the left side, and then alternated from left to right. The abdomen continued distended and rigid. The severe abdominal pain and tenderness continued for three days, then gradually disappeared, but the fever, vomiting, distention and rigidity of lower abdomen with bloody, mucous stools continued for three weeks. The patient was in bed until the middle of September; was very weak and nervous; at times he was quite hysterical, and would cry for hours. The stools continued loose, and there was some blood in every movement. In the meantime the physician had examined the feces and found ova of the *Schistosomum japonicum* present. This examination was confirmed by Dr. Hume and other physicians of central China. The patient was given arsenic, which improved his nervous condition greatly. In October, 1910, he was brought to America and put under the care of Dr. Allan Smith, of Philadelphia, who advised outdoor life for him. He was on a farm all that winter and improved greatly, gained weight, grew in height, and his nervous condition was much better. At periods of four to six weeks, however, he was still subject to slight attacks of diarrhea, with blood and mucus in the stools. In the fall of 1911 he entered school in Princeton; his general condition was good, but there were still occasional attacks of diarrhea. During the past summer these became much less frequent. He has not had an attack now since September (three months). He has had no chills at all since coming to America. His general condition continues to improve. His mother says he has taken Bland's pills for the past two years.

The patient comes to the hospital for examination and advice, anxious to know whether he is a source of danger to other students in the school.

Physical Examination. The patient is a well-developed young man, resting comfortably in bed, not in pain, of good color.

Superficial lymph nodes: Cervical, a few readily felt glands, not tender; axillary, a few just felt; right inguinal are moderately enlarged; left inguinal scarcely felt. Epitrochlear not felt.

Abdomen: Moderately full; soft; no tenderness; no masses; no rigidity.

Liver: Dulness from fifth space to costal margin in right mammary line. Edge is definitely felt 3 cm. below costal margin in right mammary line; not tender, seems firm and smooth.

Spleen: Percusses enlarged; edge is definitely felt one finger's breadth below costal margin in left mammary line; firm, not tender.

Surface: Brown "sun-burned" areas about the neck and arms. One small area 2 cm. x 1 cm. on right upper arm, scaling and slightly red.

Rectal Examination. The rectum contains a few hard fecal masses; there is no tenderness; no masses in wall of rectum; the

prostate is not enlarged or tender. Examination otherwise shows normal conditions.

December 10. Feces: A few ova of *Schistosomum japonicum* found. Faint reaction for blood.

December 11. Blood: Hemoglobin, 80 per cent.; red-blood cells 4,728,000. Differential leukocyte count: polynuclears, 81 per cent.; lymphocytes, 15 per cent.; large mononuclears, 2 per cent.; eosinophiles, 2 per cent.

Urine: 1030; acid; albumin, faint trace; glucose, none. Microscopic: a few white-blood cells; occasional hyaline casts; no blood.

December 17. A few ova of *Schistosomum japonicum* found in the feces.

December 19. Blood: Leukocytes, 19,100; polynuclears, 61 per cent.; lymphocytes, 18 per cent.; large mononuclears, 2 per cent.; eosinophiles, 19 per cent.

December 19. Patient discharged today; condition same as on admission. He has been up in a chair during a considerable part of his stay in the hospital. Temperature has varied from 98° to 100°. Pulse, 70 to 110.

The patient is advised to practise disinfection of his stools.

This case impressed upon us the possibility of the occurrence of this severe infection in Europeans and Americans living in the infected areas; it also suggested the desirability of publishing these reports, and, in view of the fact that this parasite has been known only since 1904, of gathering together all the facts regarding it to be obtained from the literature.

The African brother of this parasite, the *Schistosomum hematobium*, was discovered by Bilharz in 1851, who showed that it was the exciting agent in a disease of the genito-urinary tract since designated *Bilharzia hematobia*. This infection has come to be quite well known by reason of its widespread prevalence throughout Africa, Asia Minor, and Mauritius.

HISTORICAL NOTE (Manson). For some years Japanese physicians had observed in the provinces of Yamanashi and Hiroshima in central Japan and at Saga in the north island an endemic disease characterized by enlargement of the liver and spleen, cachexia and ascites. The patients suffered from diarrhea, their motions containing mucus tinged with blood. Occasionally they had fever. They became anemic, and many of them died of exhaustion. At autopsy the liver and other organs were found to contain the ova of some unknown helminth. As far back as 1888, Majima² in Tokio had found peculiar ova in the liver of a case of cirrhosis. These he described as the ova of an unknown parasite. In 1890, in a similar case, Yamigawa³ found ova which he ascribed to the lung

² Manson's Tropical Diseases, fourth edition, p. 663.

³ Virchow's Arch., 1908, cxlii, 325.

trematode. In April, 1904, Katsurada⁴ discovered that the ova found in the stools of these patients contained a ciliated embryo not unlike the miracidium of *Schistosomum hematobium*.

Disappointed of an autopsy, he examined dogs and cats in the endemic area, and had at once the good fortune to discover in the portal systems of two cats from the province of Yamanashi numerous *Schistosomata* containing eggs exactly similar to those previously found in man. He published this information on August 13, 1904, and named the new trematode *Schistosomum japonicum*. Almost simultaneously and independently, Fujinami⁵ observed cases of the disease in the village of Katayama in the province of Bingo, and found in his first fatal case the characteristic ova in various organs. In a second necropsy, besides the ova in the liver, intestinal wall, and mesenteric glands, he found in a branch of the portal vein a parasite which he regarded as *Schistosomum hematobium*. In November, 1904, Catto⁶ discovered the same parasite in sections of the mesocolon of a Chinaman, from the province of Fukien, who died of cholera at St. John's Island, Quarantine Station, Singapore.

GEOGRAPHICAL DISTRIBUTION OF THE PARASITE. Japan. Japanese writers (Tsuchiya) speak of the disease (schistosomiasis) as endemic in the provinces of Yamanashi, Hiroshima, and Saga. On account of the changing nomenclature of the Japanese provinces (employed by geographers) it is somewhat difficult to place these provinces accurately on modern maps, but Yamanashi and Hiroshima apparently belong to the extreme western part of the main island of the Japanese group, Hondu or Honshi, while Saga is to be found in the northern part of the adjacent islands of Kiusiu. Tsuchiya⁷ also reports finding the eggs of the parasite in two Japanese from other parts of the country, one from the province of Miye and another who had passed his life in a village near Tokio.

China: Catto's original observation of the eggs of the parasite was made on the body of a Chinaman in Singapore. Beyer,⁸ Peake,⁹ Skinner,¹⁰ Lambert,¹¹ and others report observations in a number of Chinamen in various parts of the Empire. Houghton,¹² in a comprehensive study of the disease in China, says that it has been shown to be endemic in the provinces of Hunan, Honan, Hupeh, Kiangsi, and Nganhui (Anhui), all of which lie in central China, along the valley of the great Yang-tse-Kiang. His own observations cover a territory of 100 miles about the city of Wuhu. Eight per cent. of all the males entering the Western General Hospital of that city are infected with this parasite, and in some parts 25 per cent. of the population suffer from diseases engendered by it.

⁴ Manson's Tropical Diseases, fourth edition, p. 662.

⁶ Trans. London Path. Soc., 1905, lvi, 179.

⁸ Amer. Med., 1905, x, 578.

¹⁰ Ibid., 1911, xiv, 129.

¹² Jour. Trop. Med., 1910, xiii, 185.

⁵ Ibid.

⁷ Loc. cit.

⁹ Jour. Trop. Med., 1909, xii, 64.

¹¹ China Med. Jour., 1911, p. 308.

Philippine Islands: Wooley¹³ discovered the infection in a native Filipino who had never been out of the islands and who at the time of his death was confined in the Bilbid prison.

England: Manson¹⁴ found the ova of the schistosomum in the feces of a patient (presumably an Englishman) who has spent some time in north China, and speaks of it as the first observation of the infection in an European.

United States: Our own observations given above consitute, so far as can be learned, the first cases reported in this country. They were evidently both imported. Logan¹⁵ reports the case of a boy, aged thirteen years, the son of an American missionary, who had probably suffered his infection while living at Yochow, Hunan. We are satisfied that our Case II is the same boy.

DESCRIPTION OF THE PARASITE. Like the *Schistosomum hematobium* the *Schistosomum japonicum* is a bisexual trematode, the male measuring 9 to 12 mm. in length and 0.5 mm. in breadth; the female 12 mm. by 0.4 mm. The flat body of the male is folded over to form a gyneophoric canal, into which the body of the female is received. Both sexes bear upon the anterior extremity two suckers, a small one upon the very tip, a second, larger and pedunculated, being placed somewhat posteriorly upon the ventral surface. These suckers and the ventral surface of the body of the male are provided with minute spines. The body surface of the male is otherwise smoother than that of *Schistosomum hematobium*, and rather wider in the posterior part, the sides overlapping more extensively than in the latter. In further distinction from the *Schistosomum hematobium*, Catto¹⁶ describes a larger vas deferens and lobulated testicles in the male *Schistosomum japonicum*, and a different arrangement of the yolk cells in the female. Looss¹⁷ notes a greater development of the muscular system in *Schistosomum japonicum*, which he thinks may take the place of the cuticular eminences of *Schistosomum hematobium*.

The eggs, which occur in large numbers in the uterus of the female, measure on an average 0.055 mm. in length and 0.031 mm. in breadth. They are oval shaped, pale yellow, with thin refractile capsules, smooth surface, and contain either granular material or a developing embryo, the myracidium. The ova which are found in the feces nearly always contain myracidia, and are larger than the young undeveloped ova. The embryo as it lies in the ovum is pear-shaped, with a tapering trunk and sharp-pointed proboscis. Its average dimensions are 0.074 by 0.053 mm. It is made up of cells which contain refractile granules, and its surface is covered with cilia. If one of the eggs be pressed under a cover-glass, the parasite can be seen moving about inside the shell membrane.

¹³ Filipino Jour. Science, 1906, i, 83.

¹⁴ Ibid., 1911, xiv, 133.

¹⁷ Centralbl. f. Bakt., etc., 1905, 1 Abt., Orig., xxxix, 280.

¹⁴ Jour. Trop. Med., 1908, xi, 346.

¹⁶ Loc. cit.

The eggs of *Schistosomum japonicum* are to be distinguished from those of *Schistosomum hematobium* by the following differences

1. The ova of the former parasite are the smaller. Eggs of *Schistosomum hematobium* average 0.12 mm. x 0.05 mm., twice the dimensions of *Schistosomum japonicum*.

2. The ova of *Schistosomum hematobium* possess a lateral spine; those of *Schistosomum japonicum* do not. (R. T. Leiper¹⁸ has recently published a note in which he claims to have demonstrated small knob-like spines on the ova of *Schistosomum japonicum*.)

PATHOGENESIS. The disease occurs almost exclusively among workers in rice fields and among children who bathe in the canals adjoining rice fields. In June the fields are flooded with water from the canals and then manure (human feces)—the chief source of infection—is spread over the soil. People working in the fields at this time are often taken with an unpleasant itching and rash on the parts of the body exposed to the water. Observation of these facts soon led Japanese investigators to the conclusion that the portal of entry of the infection was usually, if not always, to be found in the skin, and experiments have shown that in the case of animals, at least, infection through the skin is much more easily accomplished than infection by way of the digestive tract. Fujinami and Nakamura¹⁹ kept six healthy calves standing for several hours in flooded rice fields, with bandages over their mouths. In the control series, the legs of the calves were wrapped with oil-cloth and no gags were placed over the mouths. All six of the calves whose legs had been exposed, became infected with the *Schistosomum japonicum*, while in the control series only one showed the parasite and this one had only two foci. Similar experiments were performed with dogs and rabbits. Katsurada and Hashegawa²⁰ carried out some ingenious experiments on cats and pups. Wooden yokes were placed about their necks so as to render infection per os impossible; then the animals were put in the flooded rice fields or in the canal water. In this way they were easily infected. Attempts, however, to transmit the disease by giving them infected water proved futile. Katsurada and Hashegawa concluded from their experiments that infection with *Schistosomum japonicum* takes place solely by way of the skin. The fact that the miracidia are soon killed by 0.1 per cent. hydrochloric acid supports this view, as it makes infection through the stomach practically impossible.

Fujinami and Nakamura were unable to determine whether the parasite entered the skin in the form of the miracidium itself or whether an intermediate host was necessary for infection. More recently, however, Matsuura and Yamamoto²¹ demonstrated a *Schistosomum japonicum* larva just entering the skin, and a few

¹⁸ Jour. Trop. Med., 1911, xiv, 76.

¹⁹ Kyoto igakn Zassi, vi, Fasc. 4.

²⁰ Centralbl. f. Bakt. etc., 1910, I Abt. Orig., liii, 519.

²¹ Chugai Iai Shimpō, 1911, p. 755.

days later found larvæ similar in size and structure in the infecting water.

Location and Distribution of the Parasite in the Body. The parasite having gained entrance to the body finally takes up its abode in the portal vein and its branches. Tsuchiya²² found the parasites only in the portal vein in careful examinations made in seven cats, one dog and three men. In all 410 parasites, about equally divided between male and female, were recovered from the seven cats. Of these 150 were paired, the remainder single. Nearly all the parasites found in the mesenteric veins were in copulation, while in the portal vein or its branches many single individuals were found. Tsuchiya thinks that sexually immature parasites or those unable to find a mate remain in the portal vein or its branches in the liver; but that the copulating parasites make their way back against the blood-stream into the mesenteric veins and finally to the intestinal tract, where the eggs are deposited in the smaller vessels and capillaries. The ova do not, as a rule, remain in the capillaries, but wander out into the stroma of the mucosa and submucosa of the stomach and intestine. Here they collect in large numbers and many of them eventually break through the mucous membrane (with the production of more or less ulceration) and become mixed with the intestinal contents. The ova that remain in the tissue are attacked by leukocytes and destroyed, or they become encapsulated with fibrous tissue and undergo calcareous degeneration. Some of the ova are carried by the blood into the liver and become lodged in the capillaries there. Others find their way into the mesenteric lymph glands.

PATHOLOGY. The most constant and characteristic gross findings in *Schistosomum japonicum* infections are enlargement of the liver, spleen, and mesenteric lymph glands. In the later stages of the disease the liver may be small and hard, due to destruction of the parenchyma and contraction of the fibrous tissue. In either case the liver is quite firm and resistant; its surface is coarsely granular or nodular (Fig. 1), suggesting syphilitic cirrhosis. The older the infection the more advanced the cirrhosis. The cut surface is coarsely granular, pale yellow, and traversed in every direction by dense bands of fibrous tissue, which appear to follow the portal vessels.

Microscopically the liver shows more or less extensive new growth of fibrous tissue (Fig. 2), particularly about the portal vessels. In the meshes of the stroma the eggs of *Schistosomum japonicum* are found, sometimes well preserved, at other times compressed and atrophied. In the earlier stages of the disease there is considerable infiltration of lymphoid cells about the ova.

The spleen is hypertrophied, usually considerably so, and very

²² Loc. cit.

firm in consistence. This increase in size and consistence is due to the portal congestion and consequent proliferation of fibrous tissue. The cut surface is dark red, and oozes a small amount of pulp.

Microscopic sections show a partial replacement of the follicles by connective tissue, which has also filled up the sinuses. The trabeculae are greatly thickened, and may show hyaline degeneration. The mesenteric lymph glands are enlarged, and sections show changes similar to those observed in the spleen. Here and there in the fibrous tissue or lying free in the sinuses are found ova of *Schistosomum japonicum*.

The pathological changes in the gastro-intestinal tract are most marked in the lower portion of the small gut and the whole of the large intestine. In the gross the lesions are often not striking. In the milder cases the mucosa may show nothing more than numerous minute punctate hemorrhages of a reddish brown color. In the severer cases, hemorrhagic ulcers of various sizes occur. The mucosa becomes hypertrophied and thrown up into folds, so that in some places small polyps are formed. The serosa, especially that of the large gut, may become thickened and bound to the other viscera by fibrous adhesions. Microscopically the lesion is the same throughout the gastro-intestinal tract, varying, however, in severity. The characteristic lesion consists of a deposit of ova in the submucosa (Fig. 3), which lie embedded in granulation tissue if recently deposited, or dense fibrous tissue if of long duration. The mucosa may be intact, but more often there is atrophy, or complete destruction of the mucosa, with the formation of ulcers. The dilated veins of the submucosa give these a hemorrhagic quality. The muscularis is usually free from invasion, but the serosa often contains deposits of eggs, which produce chronic inflammatory changes and thickening of the fibrous coat.

As intimated above, the lower portion of the ileum and the entire large intestine are chiefly affected, but small groups of ova are sometimes found in the wall of the stomach, duodenum, and jejunum. In addition to these more usual locations ova are occasionally found in the lungs, spleen, pancreas, mesentery, gall-bladder, and brain (Yamagiwa).

SYMPTOMS. These may be explained as in part the results of mechanical irritation produced by the presence of the eggs of the parasite in the intestinal mucosa or other parts, such as the spleen and liver, in part the results of a hemolytic secretion of the parasites (Yagi²³), or in the terminal stages as the results of both factors. It is obvious that as in other parasitic invasions, *Ankylostomum duodenale* or *Schistosoma hematobium*, for example, infection by the *Schistosomum japonicum* may occur without resulting symp-

toms. Manson²⁴ reports his finding in a patient who had only vague digestive disturbances. In our first case it is doubtful whether the ova had anything to do with the hematemesis from which the patient died. From the mild or latent infections varying grades of disturbance up to severe dysentery, anemia, enlargement of liver and spleen, ascites, and fever may be seen. Houghton,²⁵ who has had unusual opportunities to observe the disease, classifies the cases clinically as follows:

1. Cases showing ova in stools but no bodily reaction—2 out of 40 cases.

2. Cases negative except for marked eosinophilia. These, he says, make bad surgical risks.

3. Cases presenting only splenic enlargement. These are often difficult to diagnose, if the ova are absent or scarce in the stools. An eosinophilia of over 10 per cent. he regards as suggestive—11 out of 40 cases.

4. Cases with cerebral symptoms and a high grade of eosinophilia. He had only a single case of this type, and there is no proof that the schistosomum infection was in any way related to the hemiplegia from which the patient suffered, although Yamagiwa²⁶ reports that he found the ova of *Schistosomum japonicum* in the cerebral cortex of a patient who had suffered from Jacksonian epilepsy. Tsuchiya,²⁷ in two of his autopsies, found the eggs in the lungs and pleura. Usually the parasites and their eggs are confined to the portal system, but it is obvious that if the eggs reach the lungs, they may be carried to the brain, and, lodging there, may produce symptoms.

5. Typical cases showing enlargement of the liver and spleen, dysentery (with bloody stools)—16 out of 40 cases. In this group our second case would belong. The recurrent fever with which our patient suffered is noteworthy. Such fever may be the first symptom of the disease, and only after the fever has run for some time may the other symptoms develop (Tsuchiya.)

To these groups should be added:

6. Terminal cases in which in addition to the symptoms of the preceding group the patients present evidences of portal obstruction (ascites) and advanced anemia, and die of exhaustion. One of Tsuchiya's patients had had his abdomen punctured forty-eight times in the course of three years. The ascites may be explained partly by the cirrhosis of the liver, partly by an endophlebitis and thrombosis of the veins of the portal system, excited by the eggs of the parasites. In man the parasites seem not to be present in sufficient number to directly affect of themselves the circulation of the portal system. Jaundice may be present in this stage of the disease, but appears to be a relatively rare symptom.

²⁴ Loc. cit.

²⁶ Virchow's Archiv, cxix, 447.

²⁵ Loc. cit.

²⁷ Loc. cit.

INDIVIDUAL SYMPTOMS. *Skin Eruptions.* The cutaneous phenomena described in the history of our second patient give rise to interesting questions. Have they any relation to the infection from which he was later proved to be suffering? Do they represent the results of irritation produced by the larvæ of the schistosomum? In this connection we recall with interest the observation of the prevalence of ground-itch in hook worm districts by Bentley, the occurrence of a dermatitis on Loos' hands on exposure of the skin to "cultures" of the ankylostomum larvæ, and his subsequent demonstration that these larvæ can pass the skin and ultimately by this route reach the intestinal tract. In Porto Rico, Ashford, King, and Gutierrez found that 98 per cent. of patients suffering from ankylostomum infection gave a history of the characteristic dermatitis or "mazamorro" as the natives name the affection. Skin infection has come to be accepted as at least the common path of infection in this disease, and there is, as already shown, evidence that the like situation prevails with relation to the schistosomum.

The phenomena in our patient diagnosed as angioneurotic edema appear to have had much too general a distribution to warrant the belief that they could have been caused directly (by irritation produced) by larvæ of the parasite unless the patient had been bathing in badly infected water. Of this there was no history. On the other hand the rash on the legs and arms later described developed after the symptoms of his affection had been present for more than a year, and the illness which followed developed too promptly to allow one to regard it as possibly a new infection. The possibilities presented by the skin phenomena in this case can at present be regarded only as speculations. Nowhere in the literature have we found any extended reference to such skin eruptions. Matura and Yamamoto²³ have, however, shown that the larva of *Schistosomum japonicum* may be found entering the skin and have demonstrated the presence of like objects in infected water. Lambert describes the case of a sportsman who suffered from low fever, with urticaria and a high eosinophilia, in whose stools he later found the ova of *Schistosomum japonicum*. He states his conviction that the disease occurring in the Yangtse Valley and known locally as river fever, urticarial fever, or Yangtse fever are all one and the same infection by this parasite. His remarks imply that urticaria is a common occurrence (or urticaria together with fever) in the early stages of the disease, but he does not give the details of his observations.

CIRCULATORY SYSTEM. In the later stages of the disease, edema of the ankles or a general anasarca may develop as a sequel of advanced anemia and exhaustion, but the heart and major circulation are not usually affected, and in the early stages of the disease

²³ Loc. cit.

present only such disturbances as belong to the fever and exhaustion produced by the infection.

RESPIRATORY SYSTEM. As in our first patient, Tsuchiya²⁹ found dense pleural adhesions and thickening of the pleura at autopsy. He also demonstrated hemorrhagic infarction of the lung near which individual eggs of the parasite could be found, but not in such relation as to indicate that the infarction had resulted from their presence. He, therefore, regarded it as resulting from hypostatic congestion in the terminal stage of the disease.

ALIMENTARY TRACT. In the nature of things the symptoms are mainly referred to this tract, and they may be very mild, as in Manson's patient, or so severe as to end in death.

Diarrhea is a fairly constant feature of the clinical picture. In the milder cases the diarrhea is slight, the stools are watery or soft; in the severer conditions the diarrhea is distressing, the stools containing mucus and blood. Bleeding from the bowel may be so severe as to be the cause of death. We can, however, find no reference to such an experience as we had with our first patient.

Enlargement of the liver and spleen occurs early in the disease, and appears to persist throughout. The enlargement is gradual and painless. The surface of the liver, originally smooth, may later show irregularities due to cicatricial contraction. The spleen is large, firm, and sharp-edged. Jaundice is a rare complication.

Ascites is a late development resulting from portal obstruction. It may be evanescent, disappearing in some instances after one tapping; in other cases persisting after more than forty. With ascites the veins of the abdomen may be enlarged, but they are rarely as prominent as in atrophic cirrhosis of the liver.

The enlargement of the spleen may be very marked. It occurs quite independently of the presence of parasites or eggs in the spleen itself. In the late stages of the disease it is largely due to portal congestion, and may be greatly reduced, as in our first case, by a large hemorrhage (Tsuchiya.)

URINARY SYSTEM. The urine shows no changes characteristic of the disease. The ova of *Schistosomum japonicum* never appear in the urine.

BLOOD. The changes in the blood are important. By some writers anemia is spoken of as a characteristic feature of the disease. It is evident that if bleeding from the alimentary tract be persistent, progressive anemia must follow. Houghton and others, however, speak of anemia as rather an infrequent result of the infection. Eosinophilia appears to be almost constantly present, as in infection with other parasites. Lambert³⁰ says that the eosinophilia may amount to 60 per cent. of the leukocytes. The leukocytes may be, but are commonly not, increased in total number. In anemia

²⁹ Loc. cit.

³⁰ Loc. cit.

the red blood cells and hemoglobin are both reduced, but the latter to a greater degree, as in any secondary anemia.

DIAGNOSIS. In the districts where the disease is endemic Lambert asserts that the diagnosis can be made before the appearance of ova in the stools on the following points:

1. A history of bathing or wading in shallow ponds or rivers in the vicinity of the Yangtse River, followed, if only one prolonged contact with infected water has occurred, by:

2. An incubation period of ten to fifteen days.

3. Fever 100° to 102° and sweating.

4. An eosinophilia possibly amounting to 60 per cent.

It is quite evident that while these points may suffice to identify the affection under special conditions, they cannot be relied upon to do so at all times. Apart from the history of exposure to infected water the phenomena would suggest trichinosis quite as strongly as infection with the *Schistosomum*. If the antigen were more easily obtained, the complement fixation reaction could be employed, for Yoshimoto³¹ has shown that it affords an accurate means of diagnosing Schistosomiasis.

The only conclusive clinical evidence of this infection must be the finding of the ova in the stools. The points of distinction of these have already been given. They are almost identical with the ova of *Schistosomum hematobium*, but may be differentiated from them by their smaller size and the absence of the lateral spine.

The ova are usually found without much difficulty, though in our second case some specimens of feces failed to show any. We made the observation that ova were more numerous in stools that contained blood than in those that were free from it.

PROGNOSIS. As to life, prognosis is good; as to health, bad. No exact statistics of mortality are available. Katsuura says that he had seen from 30 to 54 cases in each of five years, and of these numbers from 3 to 5 would prove fatal. He thought it probable that the indirect mortality of the disease would be much higher.

The duration of life varies greatly. In the worst cases it appears to be several years before the patients succumb. Under more favorable conditions life may be protracted twenty to thirty years. Two of Tsuchiya's patients were between sixty and seventy years of age; one had led an active life for thirty years after the onset of symptoms.

In fatal cases death resulted either from exhaustion consequent to persistent ascites and repeated paracentesis, or hemorrhage, or complications induced by the increased abdominal pressure.

PROPHYLAXIS The evidence at present is that the miracidium is the dangerous form of the parasite. If its development is checked, or its ingress into the skin prevented, infection fails. The important

³¹ Zeitsch. f. Immunitätsf., etc., 1910, Orig., v, 438.

steps, therefore, appear to be the prevention of the access of the miracidium to fresh water or the contact of infected water with the human skin. How difficult these steps may be in such districts as the Yangtse Valley appears at once, when we learn that all through China and Japan fresh human feces is used as fertilizer, and that thousands of people who make their living as fishermen, lumbermen, boatmen, etc., as well as those who occasionally wade or bathe in lakes or rivers, are exposed to infection.

Yet the situation is not entirely hopeless. There is evidence that if prevented from reaching fresh water even for a few days the miracidium dies and the danger of infection ceases. The general adoption of water-tight latrines or vaults in which the feces could be retained for a time would meet the requirements of the situation. Of course, the proper disinfection of the feces by formaldehyde, lime, or any other active disinfectant would also be effective, but such measures are practically useless among a population innocent of all knowledge of sanitation.

For the European the important point appears to be the avoidance of bathing or wading in shallow streams, lakes or ponds in the infested district. Doubtless there is some danger in exposure of the skin to any untreated water, but this appears to be remote except under the special conditions noted.

The full explanation of these facts in the life-history of the miracidium has not yet been worked out. Under conditions of life in this country there appears to be very little danger of the spread of infection. Yet the possibility cannot be denied, if the discharges of infected persons are allowed to contaminate small streams, in which other persons bathe or wade. Disinfection of the stools of every one known to be suffering from the disease must therefore be required.

Since the exact route of infection is still a moot question, it goes without saying that all persons living in an area where schistosomiasis is endemic should drink only carefully filtered or boiled water.

TREATMENT. Removal from the zone of danger is advised, as this will at least prevent reinfection. It is believed that in time the parasites die out, the eggs are evacuated or encysted, and if the patient survives the disease becomes quiescent. Diarrhea within certain limits is not harmful, but rather a method of elimination. Our efforts, therefore, must be directed toward careful feeding to prevent loss of weight and strength, the administration of iron to correct the anemia, and such general tonics as may be indicated. If ascites develops, tapping relieves it, and it may not return. In the earlier stages it may be met by restriction of fluids, a low-salt diet and saline catharsis, as in cirrhosis of the liver.

THE ABSENCE OF HYPERPLASIA OF THE REMAINDER OF THE
THYROID IN DOGS AFTER PIECEMEAL REMOVAL OF
THIS GLAND. AUTO-TRANSPLANTATION OF THE
THYROID IN PARTIALLY THYREOIDE-
TOMIZED ANIMALS.

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I WOULD here express my thanks to Dr. Halsted,¹ at whose suggestion these experiments were conducted.

Dr. Halsted in 1887 and 1888 showed that in dogs hypertrophy took place in the remaining gland after small pieces of a lobe had been removed.

In the experiments which follow, the manner in which the wounds healed did not seem to affect in any way the behavior of the remainder of the thyroid in the necks of the dogs.

The operation of piecemeal removal was performed on 39 dogs, and the wounds, with few exceptions, healed absolutely *per primam*. Only in one of these 39 dogs did the remainder of the thyroid present a picture of marked glandular hyperplasia.

In 20 dogs the wounds were left open to heal with suppuration. Neither hyperplasia nor hypertrophy were observed in the remaining thyroids of these dogs. Hypertrophy is used to denote measurable increase in the size of the remaining thyroid; hyperplasia signifies changes in the histological picture.

THE EFFECT UPON THE REMAINING GLAND IN THE 39 DOGS OF THE ASEPTIC SERIES, TABLE 1. Dogs 1 to 11; 101 to 124; 501; 701 to 703. In this series the pieces removed at the first operation varied in size. The largest amount removed at the first operation was one and three-quarter lobes; the smallest was approximately one-fifth of one lobe.

In dogs Nos. 120, 121, 123, 124, and 501 no transplantations were made at the first operation; in the remaining 34 dogs auto-transplantation was the invariable rule at the first operation.

Of 36 dogs only 3 of the pieces obtained at the second operation or at autopsy differed microscopically from the pieces removed at the first operation. In these three dogs the change was from early glandular hyperplasia to normal.

¹ Dr. Halsted in a paper on Reconsideration of the Question of Experimental Hypertrophy of the Thyroid Gland, and the Effect of Excision of this Organ upon Other of the Ductless Glands, delivered before the Congress of Physicians and Surgeons, Washington, May, 1913, alluded to the experiments which are herewith reported. See Amer. Jour. Med. Sci., 1914, No. 1, vol. clxvii, p. 58 and 59.

Dog No. 1. The inferior fourth of the left lobe removed at the first operation showed early glandular hyperplasia. The piece removed 81 days later at the second operation was normal.

Dog No. 9. The inferior one-fourth of the left lobe removed at the first operation showed early glandular hyperplasia. The piece removed 66 days later at the second operation was normal.

Dog No. 102. The inferior one-fourth of the left lobe and the inferior two-fifths of the right lobe removed at the first operation showed early glandular hyperplasia. The pieces obtained when the animal was sacrificed 94 days after the first operation were found to be normal.

There was no change in the structure of the remaining gland in 33 dogs during the intervals between the first and second operation or autopsy. The intervals between the first and second removals were: 41, 41, 62, 64, 30, 42, 84, 66, 96, 114, 21, 21, 61, 50, 22, 30, 15, 16, 21, 83, 84, 75, 23, 59, 57, 30, 23, 20, 20, 34, 87, 33, and 62 days.

The specimens removed from the following three dogs at the first operation were lost.

Dog No. 109. The pieces obtained at autopsy 24 days after the first operation were normal in structure. Amount of privation at the first operation was one lobe.

Dog No. 118. One and one-third lobes removed at first operation. Piece removed 58 days after first operation was normal.

Dog No. 122. Two-thirds of one lobe removed at first operation. Piece removed 153 days after first operation was normal.

The remaining glands in 18 dogs did not undergo a change in size or structure during the intervals between the second and third operations, or during the intervals between the second operations and autopsies. The intervals between the second and third operations or autopsies were: 71, 105, 129, 95, 80, 85, 63, 94, 84, 51, 42, 54, 55, 24, 54, 25, 12, and 25 days.

In one dog the remaining gland removed at the third operation showed a structural change:

Dog No. 114. The inferior fifth of the right lobe removed at the first operation was normal. At operation II, 84 days after first operation, the entire left lobe and one-half of the remaining four-fifths of the right lobe were removed. Total privation, one and three-fifths lobes. The pieces removed at the second operation were normal. The remaining two-fifths of the right lobe removed when the animal was sacrificed 53 days after the second operation, 137 days after the first operation, had not increased in size, but on examination presented a picture of marked glandular hyperplasia.

The small piece of one lobe remaining to each of 8 dogs at the fourth operation had, with two exceptions, undergone no change in size or structure.

In six dogs (Nos. 1, 2, 3, 4, 5, and 7) the pieces obtained at the

fourth operation presented the same histological picture as those from the third operation. The intervals between the third and fourth operations were: 98, 104, 79, 91, 101 and 58 days. The total number of days between the first and fourth operations on these dogs were: 250, 251, 249, 248, 245, and 185 days.

Dog No. 1. Operation I. Deprived of one-fourth of left lobe. Diagnosis: early glandular hyperplasia. Operation II, eighty-one days after the first, deprived of remaining three-fourths of left lobe. Diagnosis: normal. Operation III, seventy-one days after second, and 152 days after first operation, deprived of two-thirds of the right lobe. Diagnosis: normal. Total privation now one and two-thirds lobes. Operation IV, 98 days after third and 250 days after the first operation. Remaining one-third of right lobe removed. Diagnosis: normal.

Dog No. 2. Operation I. Inferior one-third of left lobe removed. Diagnosis: normal. Operation II, 41 days after first, remaining two-thirds of left lobe and the inferior one-fifth of right lobe removed. Diagnosis: normal. Total privation, one and one-fifth lobes. Operation III, 105 days after the second and 146 days after the first operation, two-thirds of the remaining four-fifths of the right lobe removed. Total privation, one and eleven-fifteenths lobes. Diagnosis: normal. Operation IV, 104 days after the third and 250 days after the first operation, the remaining four-fifteenths of right lobe removed. Diagnosis: normal.

Dog No. 3. Operation I. Inferior one-half of left lobe removed. Diagnosis: normal. Operation II, 41 days after first, the remaining one-half of left lobe and the inferior one-half of right lobe removed. Diagnosis: normal. Amount of privation, one and one-half lobes. Operation III, 129 days after the second and 170 days after the first operation. One-third of the remaining one-half of right lobe removed. Amount of privation, one and two-thirds lobes. Diagnosis: normal. Operation IV, 79 days after the third and 249 days after the first operation. The remaining one-third of right lobe removed. Diagnosis: normal.

Dog No. 4. Operation I. Entire left lobe removed. Diagnosis: normal. Operation II, 62 days after the first. Inferior one-fifth of right lobe removed. Diagnosis: normal. Amount of privation, one and one-fifth lobes. Operation III, 95 days after the second and 157 days after the first operation. One-third of the remaining four-fifths of the right lobe removed. Diagnosis: normal. Amount of privation, one and seven-fifteenths lobes. Operation IV, 91 days after the third and 248 days after the first operation. Remaining eight-fifteenths of right lobe removed. Diagnosis: normal.

Dog No. 5. Operation I. Inferior half of left lobe removed. Diagnosis: normal. Operation II, 64 days after the first. The remaining one-half of left and one-half of the right lobe removed. Diagnosis: normal. Amount of privation, one and one-half lobes.

Operation III, 80 days after the second, 144 days after the first operation. One-third of the remaining one-half of right lobe removed. Diagnosis: normal. Amount of privation, one and two-thirds lobes. Operation IV, 101 days after the third and 245 days after the first operation. The remaining one-third of right lobe removed. Diagnosis: normal.

Dog No. 7. Operation I. Entire left lobe removed. Diagnosis: early glandular hyperplasia. Operation II, 42 days after the first. Inferior one-fourth of right lobe removed. Diagnosis: early glandular hyperplasia. Amount of privation, one and one-fourth lobes. Operation III, 85 days after the second and 127 days after the first operation; one-half of the remaining three-fourths of the right lobe removed. Diagnosis: early glandular hyperplasia. Amount of privation, one and five-eighths lobes. Operation IV, 58 days after the third and 185 days after the first operation. Remaining three-eighth of right lobe removed. Diagnosis: early glandular hyperplasia.

The remaining gland in two dogs (Nos. 9 and 11) showed a structural change at the fourth operations; a change from normal to early glandular hyperplasia.

Dog No. 9. Operation I. Inferior one-fourth of left lobe removed. Diagnosis: normal. Operation II, 66 days after the first operation. Remaining three-fourths of left lobe and one-third of right lobe were removed. Diagnosis: normal. Amount of privation, one and one-third lobes. Operation III, 94 days after the second and 160 days after the first operation. Two-thirds of the remaining two-thirds of right lobe removed. Diagnosis: normal. Amount of privation, one and seven-ninths lobes. Operation IV, 76 days after the third operation and 236 days after the first. Remaining two-ninth of right lobe removed. Diagnosis: very early glandular hyperplasia.

Dog No. 11. Operation I. Inferior one-third of left and inferior one-third of right lobe removed. Diagnosis: normal. Operation II, 96 days after the first operation. The remaining two-thirds of the right lobe and one-fourth of the remaining two-thirds of the right lobe removed. Diagnosis: normal. Amount of privation, one and one-half lobes. Operation III, 51 days after the second and 147 days after the first operation; one-fifth of the remaining one-half of right lobe removed. Diagnosis: normal. Amount of privation, one and three-fifths lobes. Operation IV, 39 days after the third and 186 days after the first operation. The remaining two-fifths of right lobe removed. Diagnosis: very early glandular hyperplasia.

BEHAVIOR OF THE REMAINING GLAND IN DOGS WHOSE NECK WOUNDS WERE LEFT OPEN AND HEALED WITH SUPPURATION. Table II. Dogs 301 to 320. The operation of piecemeal removal was performed by cutting through hair and skin, observing no

aseptic precautions and leaving the wound open. All of the cervical wounds in the dogs of this series healed with suppuration.

In this series of 20 dogs, the pieces removed at the first operations were diagnosed as follows: normal, 9; very early glandular hyperplasia, 2; early glandular hyperplasia, 7; marked glandular hyperplasia, 2.

The sizes of the pieces removed at the first operation varied from one-fifth of one lobe to one and five-twelfths lobes. The longest interval between the first and second removals was 58 days; the shortest interval 10 days. The diagnoses of the respective pieces removed at the second operation were the same as the diagnoses of the pieces removed at the first operation on the same dogs, except in two cases.

Dog No. 311. Operation I. Left lobe removed. Diagnosis: early glandular hyperplasia. At autopsy 31 days later the remaining right lobe was found to be normal in structure.

Dog No. 314. Diagnosis of left lobe removed at first operation: early glandular hyperplasia. Diagnosis of the remaining right lobe removed 50 days after first operation: normal.

No change in size or structure was observed in the pieces of the remaining glands from 18 dogs removed at the second operation. The intervals between the first and second operations were: 40, 10, 41, 14, 29, 37, 18, 22, 49, 42, 11, 50, 45, 26, 52, 52, 58, and 52 days.

In dog No. 301, a piece of the remaining left lobe removed at the third operation, 90 days after the first, showed no change in structure or size.

In Dog No. 303 (58 days' interval between the first operation and sacrifice of the dog), the remaining one-half of right lobe showed no change in structure or size.

In Dog No. 306 (76 days' interval between the first operation and sacrifice of the animal), the remaining right lobe showed no change in size or structure.

Dog No. 319 gave birth to five puppies 54 days after one and five-twelfths lobes had been removed. The remaining seven-twelfths of the right lobe, obtained when the animal was sacrificed 4 days after delivery, showed no change in size or structure. Diagnosis of pieces first removed: normal. Diagnosis of pieces obtained when the dog was sacrificed 58 days after the first operation normal.

AUTOTRANSPLANTATION OF THE THYROID GLAND.

Of forty-two transplantations, nineteen were successful. The amount of privation of thyroid gland in the animals yielding the living graft varied from one-fifth of one lobe to one and seven-ninths lobes.

Two-thirds of one lobe were removed from dog No. 11, and a portion of this piece was transplanted at the same operation. The graft was not removed at the second operation nor at the third, when the gland in the neck was reduced in amount to four-fifteenths of one lobe. The graft was obtained at the fourth operation when it had been in the abdominal cavity wall for six months; it had changed from normal to very early glandular hyperplasia. The four-fifteenths of the one remaining lobe in the neck of this dog had undergone the same change.

The oldest graft was obtained from dog No. 9, approximately seven and one-half months after implantation and had changed from normal to very early glandular hyperplasia. The thyroid in the neck had been reduced from one and three-fourths lobes to two-ninths of one lobe.

Two implantations were made into dog No. 122 at the first operation when two-thirds of one lobe had been removed. These grafts were recovered five months and twenty-five days after implantation, when there remained to the dog only two-thirds of one thyroid lobe.

The transplantation of round cylinder-shaped pieces of gland, obtained by using a sharp punch, gave the most convincing results. These pieces of gland were uniform in size and measured 5 x 4 mm.

Grafts at body temperature placed into freshly made pockets which contained no blood yielded the best results. After cutting through the anterior sheath of the rectus abdominis muscle, the median border of the muscle was pushed aside and a pocket made by opening and closing the jaws of a fine-pointed artery clamp. Great care was taken to maintain a bloodless dissection.

THE EFFECT OF AUTOTRANSPLANTATIONS UPON THE CERVICAL THYROIDS.

No transplantations were made in the 20 dogs of the series in which no antiseptic precautions were observed. Table II, dogs 301 to 320. Not in one of these dogs did the remaining gland undergo a structural change after pieces of various sizes had been removed.

No transplantations were made in 5 dogs of the aseptic series: Nos. 120, 121, 123, 124, and 501. The intervals between the first operations and autopsies were 30, 23, 20, 20, and 34 days. The control specimens removed at the first operations in these dogs were the same structurally as the pieces obtained when the animals were sacrificed.

In 23 dogs the grafted tissue was absorbed.

The greater part of the one-fourth of the left lobe removed from dog No. 1 at the first operation was transplanted. This graft had

been completely absorbed when searched for at the second operation 81 days after the first. A greater part of the remaining three-fourths of the left lobe was transplanted at the second operation. This graft when searched for 169 days after implantation could not be found.

Dog No. 2. A greater part of the remaining two-thirds of the right lobe removed at the second operation was transplanted. The graft when searched for at the fourth operation 209 days after the second had been absorbed.

Dog No. 3. Graft transplanted at first operation and searched for at the second operation 41 days after the first had been absorbed. Operation II. No transplantation. Operation III. A small piece of the piece removed from the remaining one-half of the right lobe was transplanted. This graft, 79 days later, had been entirely replaced by connective tissue.

Dog No. 4. The three transplants were absorbed. They were searched for 62, 95, and 91 days after implantation.

Dog No. 5. Greater part of the one-half of the left lobe removed at the first operation was transplanted. Operation II, 64 days after the first. No trace of graft. Greater part of one-half of right lobe transplanted. Operation III, 80 days after the second. Graft replaced by connective tissue.

The control specimens of thyroids removed from 10 dogs at the first operations were hyperplastic (dogs Nos. 1, 7, 9, 10, 101, 102, 105, 110, 113, and 701). Transplantation was the rule at the first operations on these dogs with hyperplastic glands. In 3 of the 10 dogs the remaining thyroid in the neck of the animals changed from the hyperplastic type to normal. The grafts in 2 of the 3 dogs were absorbed, while in the third a living graft was obtained when the dog was sacrificed (Dog No. 9). In 7 of the 10 dogs the grafts were absorbed, except in one case, dog No. 113. The graft in this dog was in a perfect state of preservation when removed 137 days after implantation. There was no change in the grade of hyperplasia in the remaining cervical thyroids of the 7 dogs in question, hyperplastic at the first and last removals.

Two experiments (dogs Nos. 9 and 11) tend to show that the grafted thyroid undergoes a change in structure similar to the change in the remaining thyroid in the neck of the dog.

Dog No. 9. Two grafts in this dog changed from normal to very early glandular hyperplasia during the interval between the third and fourth operations. The remaining two-ninths of the right lobe underwent the same change.

Dog No. 11. The remaining two-fifths of the right lobe and the graft in this dog changed from normal to very early glandular hyperplasia during the interval between the third and fourth operations.

THE ACCESSORY THYROIDS IN DOGS PARTIALLY DEPRIVED
OF THE THYROID GLAND.

Accessory thyroid glands were searched for and found in dogs 9, 11, 101, 113, 114, 118, 306, 318, 230, and 701. The accessory thyroids always presented precisely the same histological picture as the remains of the thyroid gland in the neck.

SUMMARY.

1. One and three-fourths of the dog's thyroid gland may be removed without appreciably affecting the remainder of the gland.

2. In only 3 of the 59 dogs on which the operation of piecemeal removal was performed did the remaining gland change from a normal to a hyperplastic state. Dogs Nos. 9, 11, and 114.

3. In 5 of the 59 dogs the remaining gland reverted from the early hyperplastic state to the normal state. Dogs Nos. 1, 9, 102, 311, and 314.

4. Where a diagnosis of some degree of hyperplasia was made at the first operation, the pieces removed from the same dogs at subsequent operations had not undergone further hyperplasia.

5. Of the pieces removed from 56 dogs at the first operation, 58 per cent. were normal, 32 per cent. showed early glandular hyperplasia, 5 per cent. marked glandular hyperplasia, and 5 per cent. very early glandular hyperplasia.

6. Definite increase in the size of the remaining gland (hypertrophy) was not observed.

7. The remains of the thyroid lobes, the accessory thyroids, and the successful grafts in a given dog, presented the same histological picture.

8. In no dog was myxedema or tetany observed in which as much as one-fourth of the thyroid and one parathyroid gland were preserved.

PITUITARY DISEASE: A CLINICAL STUDY OF THREE CASES.

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THE main purpose of this paper is to record and comment upon several cases of pituitary disorder which present noteworthy clinical features. The literature of this complex subject has become so extensive that an attempt to epitomize it cannot be made here.

Much careful clinical observation and animal experimentation is still necessary to solve the hypophysis problem, especially in its interglandular correlations and in its role in the "sex-levelling" process.

Since Marie first directed attention in 1886 to this hidden gland as a factor in disease, it has been subjected to so much scrutiny that it is in danger of becoming overworked as a *causa morbi*. The association of destructive and atrophic lesions of the hypophysis with clinical manifestations is close. The dependence of dystrophia adiposogenitalis—typus Froehlich—on hypopituitarism may be considered as proved. This form, which is characterized by defective development of secondary sexual characteristics,



FIG. 1, A. B.—Sella measures 12 x 16 mm.,. Note thin retroposed and retroverted cantel. The skiagraph was taken from a normal male, aged forty-eight years, who suffered from migraine.

atrophic genitalia, hypotrichosis, and adiposity, has its prototype in animal experimentation. Cushing¹ says: "Our first experience, therefore, with hypophysectomized adult canines deprived of all but a fragment of the pars anterior disclosed a clinical syndrome with adiposity, increased sugar tolerance, lowered body temperature, and reversive sexual changes as its chief features. Later experiences, with the production of corresponding hypophysial defects in puppies, disclosed a similar syndrome, with a persistence of sexual

¹ The Pituitary Body and its Disorders, Philadelphia, 1912.

infantilism and the additional factors of skeletal undergrowth and evident psychical disorders."

The case is different in acromegaly. Although circumstantial evidence for a hyperpituitarism or perverted secretion of the pars anterior as its cause is most conclusive, yet it is not absolute. The operative experience of Hoehenegg and Exner in acromegaly approaches the experimental in the definiteness of results.²

The case is much the same with gigantism, and as a working hypothesis, we must accept the dictum of Launois and Roy that gigantism is acromegaly in subjects whose epiphyseal cartilages are not ossified no matter what the age.

The sequence of hypophysial struma and disturbed sexual or skeletal development is not invariable. This is shown by one of our cases in which an eroded sella, 12 mm. x 16 mm. (Fig. 1), was found in a medium-sized man, aged forty-eight years. The only possible growth anomaly was delicately shaped hands and fingers. His sexual development and sexual life have been normal. The patient had long been a sufferer from proxysmal headaches, which were relieved after alkalization thoroughly carried out over a period of several years. Such cases must make us accept with reserve sellar deformity and enlargement, *i. e.*, hypophysial struma, as proof of dyspituitarism in seeking for an explanation of clinical facts.

The relationship of the pituitary gland to diabetes mellitus and insipidus will be taken up after the case reports.

CASE I.—A. L., aged sixty-one years, came under observation in January, 1908. In August, 1907, after a hard day's work in a cold-storage room he suddenly became weak, dizzy, and faint; a hemoptysis of one pint of bright red blood followed. A second hemorrhage occurred the same evening after he had entered St. Joseph's Hospital. For three weeks he spat blood daily and was much troubled with weakness and drowsiness. An intermission of about two months was followed by another hemorrhage brought on by heavy lifting. He then reentered the hospital, where he has since remained as an orderly.

During the winter of 1908 he had many attacks of the following description: After a couple of days of malaise, weakness, intense parietal headache, tinnitus aurium, vertigo, palpitation, and of periocular edema a sudden rise in temperature (102° to 104°), with hemoptysis, would occur. At such times an area 4 to 10 cm. in diameter of impaired resonance with fine moist rales could be demonstrated in the lungs. The area was always sharply localized and usually to be found posteriorly in the upper part of one of the

² Hoehenegg, J., Operativ geheilte Akromegalie bei Hypophysentumor, Verhandl. d. Deutsch. Gesellsch. f. Chir., 1908, vol. xxxvii, pp. 80 to 85; Exner, A., Rückgang der akromegalischen Erscheinungen nach Operation eines Hypophysentumors, Wien. klin. Woch., 1909, vol. xxii, pp. 108 to 109.

lower lobes. With the onset of hemoptysis the edema of the eyelids would rapidly disappear. The hemoptysis and temperature would cease two or three days later. These attacks occurred at frequent intervals for four months, when only an evanescent edema of the eyelids reoccurred at intervals of decreasing frequency. The leukocytes during the attacks varied from 7100 to 9000. A conjunctival tuberculin test and repeated sputum examinations for tubercle bacilli were negative. Repeated physical examinations during the intermissions revealed nothing except a moderate pulmonary emphysema and rapidly enlarging finger tips, which were at first considered to be a osteopulmonary arthropathy. Six months later the marked changes which had taken place in his hands, feet, and face, the increase in weight, the kyphosis, etc., made the clinical diagnosis of acromegaly certain.

At present (January 14, 1914) the patient complains merely of occasional swelling of the eyelids and slight attacks of weakness and drowsiness, which pass quickly on lying down.

Status Præsens. The patient is a large, heavy-set, elderly man (since the onset of his trouble his weight has increased from 140 to 265 pounds), the countenance is conspicuous for its prognathism, prominent cheek bones, squareness, beetling shaggy eyebrows, thick lips, muddy, pasty complexion, and apathetic expression. There is distention of the supra-orbital veins, which becomes evident on exertion or excitement. The palpebral fissures are narrow, the fundi are normal, the teeth are poor, and the tongue is normal in size. The trunk, legs, and arms are massive, the hands and feet are spade-like, the phalanges are thick, heavy, and bulbous. There is a marked increase in subcutaneous fat, and the abdomen is pendulous. There is a well-defined kyphosis of the cervicodorsal spine. There is no adenopathy, no increased area of thymic dulness, and no pigmentation. The thyroid, tonsils, and testicles are small (his sexual potency has always been very low). Perimetric examination reveals contraction, especially of the temporal fields, and a moderate interlacing of the color fields. The sella measures 17 x 11 mm., (Fig. 2). The dorsum epiphii is retroposed and retroverted. The posterior clinoid processes are thickened. The sphenoparietal sinuses with their branches are especially marked. The dentations of the lamboid suture are large and the digital impression are rather better defined than usual.

The patient took 400 grams of levulose at one time without excreting sugar. The most interesting features in this case are the peculiar angioneurotic edema of the periocular structures and the striking pulmonary phenomena. The character of the sputa and the dulness suggested infarct. The absence of cause for infarction and of disturbed general pulmonary circulation pointed rather to either an ephemeral pneumonia or an evanescent, intense, localized hemorrhagic edema of the lungs. Pneumococci were

not found in the sputa in any numbers, and the clinical course, observed during repeated attacks, was not that of abortive pneumonia. The best explanation is that it was a process similar to and of the same etiology as the edema of the eyelids, which always preceded or accompanied the lung manifestations. The anatomical lesion must have consisted of *congestion of a sharply localized lung area, with extravasation of blood and serum into the alveoli* extensive enough to impair resonance. Whether the association of the above-described syndrome with hypophysis disease is of any significance must be determined by other observations.

His subnormal sexual life and development as suggestive of a veiled hypopituitarism persisting until his fifty-sixth year is also of interest.

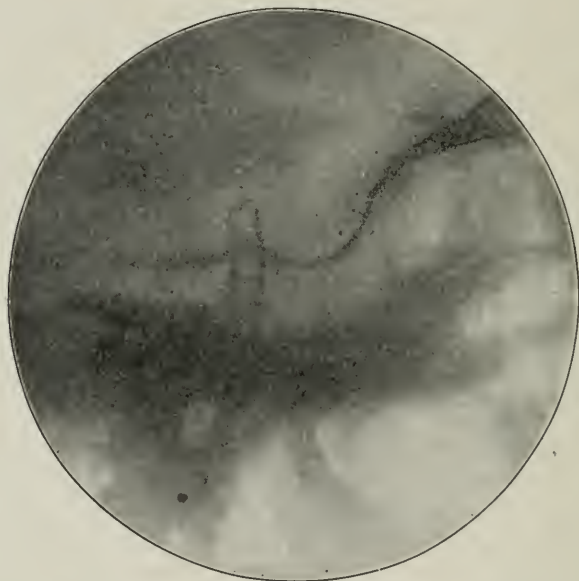


FIG. 2, A. L.—Acromegalic. Sella measures 11 x 17 mm. Note the retroversion, the retroposition, and the thickening of the dorsum epiphysii. The sella also appears "dished."

CASE II.—M. V., aged twenty years, consulted me April 4, 1909, for amenorrhea and for *transitory disturbances in her ability to express her thoughts in words*. There had been four such "spells" in the preceding three months. She had suffered an epileptiform attack the preceding day, followed by a dazed state and severe headache. The right arm was limp for a few moments. There was nothing of significance in the family or previous history.

Physical examination showed a large, fat girl with undeveloped breasts; there was no pubic or axillary hair; there was a slight

congenital asymmetry of the face; the eye muscles and fundi were normal; the power of the dorsal flexors of the right foot was diminished; the knee- and ankle-jerks were sharper on the right side, and there was a positive Babinski on the same side. There was no adiadokokinesis or Romberg's sign; the abdominal reflexes on the right side were diminished; the uterus was infantile. Otherwise the physical examination showed nothing of significance. A diagnosis of *intracranial neoplasm affecting the hypophysis—typus Froehlich*—was made.

July 30, 1910. The following notes were made: The patient has grown very rapidly during the past year. Nocturnal epilepsy has been common. The face was large, the skin coarse, and the expression stupid. The hands and feet were large and long, and the jaw was undershot. There had been a slight development of the pubic hair. The right masseter seemed weaker than the left. The examination of the nervous system revealed the same findings as formerly. The patient was put on pituitrin (P. D.) m x , t. i. d.

December 1, 1911. The menses have been practically normal since the pituitrin was started. The pubic and axillary hair have developed moderately. Headaches, vomiting, and attacks of unconsciousness have been less than formerly.

September 28, 1912. The following was noted: The patient has only missed two menstrual periods in the last two years. She has become much heavier and more obese. The features have grown coarser and cerebration very slow. She complained of frequent attacks in which she became dazed and everything seemed unreal—*uncinate attacks without olfactory aura*. The acromegalic features were marked. There was a considerable amount of spotted brown pigmentation all over the body, which had appeared since last seen (adrenal insufficiency). There was weakness and slight spasticity of the muscles of the right upper and lower extremities. The tendon reflexes on the right side were all increased; Babinski, Oppenheim, and Gordon reflexes were all present on this side. The abdominal reflexes on the right side were gone. The facial muscles were distinctly weaker on the right side; the fundi were normal; perimetric examination showed interlacing of the color fields and contractions of all of the fields, especially on the temporal side; 150 grams of levulose, 350 grams of levulose, and 400 grams of glucose were given on different days and the urine collected; there was no glycosuria.

The sella measures 13 x 15 mm. (Fig. 3). The triangular excavation into the sphenoidal cells is noteworthy. The digital impressions were specially well marked in this case. The unusual shape of the sella and the secretory phenomena would lead one to suspect an infiltrating growth arising from the hypophysis, although the focal symptoms would point rather to an *interpeduncular growth which interfered with the infundibulum and consequently*

with the cerebrospinal fluid. The osseous overgrowth associated with increase in carbohydrate tolerance is significant, inasmuch as diminution in carbohydrate tolerance has been frequently noted in hyperpituitarism.³ The transition of a hypopituitarism of the Froehlich type into a hyperpituitarism resulting in acromegaly is striking—hyperactivity of the anterior lobe with deficiency of the posterior lobe—and demonstrates the clinical existence of disassociation of the anterior and posterior lobes.

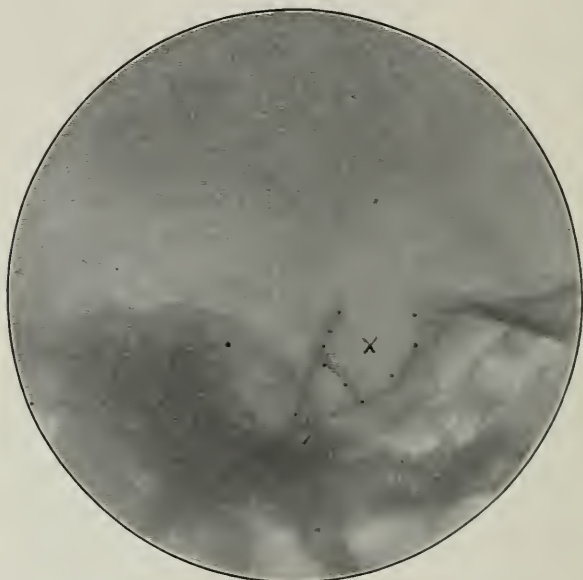


FIG. 3, M. V.—Sella measures 13 x 15 mm. Note the peculiar pyramidal shape which suggests erosion of the floor by an infiltrating process.

CASE III.—Mrs. N. was referred to me by Dr. Dierker, of Lawrence, September 1, 1913. She is twenty-three years old, has been married four years, has borne two healthy children, and has had no miscarriages. The family and past histories were negative. The present complaint began one year ago, four months after parturition. The onset was gradual, and the first thing noticed was that she was inclined to mope in a corner and show marked mental sluggishness.

The patient complained only of tiring easily and of attacks of dizziness, weakness, and depression, which come on suddenly. During the past year she has gained forty pounds, and a marked

³ Cushing, loc. cit.; Ravault, Bull. et mém. Soc. méd. d. hôp. de Paris, 1900, vol. xvii, pp. 352 to 360; Borchardt, L., Funktion u. funktionelle Erkrankungen der Hypophyse, Ergebnisse der innere Medizin u. Kinderheilkunde, 1910, vol. iii; Leri André, Akromegalie, innere Sekretion u. Nervensystem, Berlin, 1913, pp. 281 to 313.

change has taken place in her facial contour. There has been no gastro-intestinal, genito-urinary, or cardiovascular disturbances. She has suffered occasionally from occipital headaches.

The menses began at the age of fourteen years, and have always been normal. She married at the age of nineteen, and her husband states she was sexually undeveloped, and that there was no intercourse during the first year of marriage.

The patient was a large, dull, heavy-set, obese, apathetic young woman; she took little interest in her surroundings, and was unreasonable and inclined to be peevish and unruly; she would laugh or cry by the hour or sit as if in a trance. One day she spent two hours looking out of the window without changing position. Her face was square, the supra-orbital ridges were prominent, and the cheek bones protruded rather conspicuously; the face was flattened and heavy, but there was no special prognathism; the tongue was not thickened. The body was massive; the subcutaneous fat was abundant; there was a moderate growth of genital and axillary hair, with quite a little hair scattered along the linea alba. Examination of the heart, arteries, abdomen, and reflexes revealed nothing abnormal; there were no sensory disturbances; the urine was normal, although the daily output was only 400 to 600 c.c. Satisfactory perimetric observations could not be made.

The following tests to determine the carbohydrate tolerance were made: 150 grams of glucose were given in tea; on the second day 300 grams of glucose were given in tea; on the third day 450 grams were given in lemonade. After each administration the urine was collected for eight hours. In none of the tests was a reducing substance found. Marked diminution of urine was noted while these tests were in progress.

The sella measured 10 x 13 mm. (Fig. 4). There is some retroversion of the cantel, and the posterior clinoid processes seem thickened.

Fifteen minims of pituitrin (P. D.) were given hypodermically A.M. and P.M. This resulted in considerable loss of weight and a notable improvement in her mental condition.

The sexual history of the patient is important. The possibility of an antecedent hypopituitarism, manifested by complete absence of libido, with normal procreative functions, is of interest. Sexual intercourse was granted only at rare intervals, and then under protest. The lack of interest in husband, home, children, and in her wifely duties in general was significant. The husband believed her mentally unsound, and desired that she be committed; therefore the case assumes a medicolegal aspect. A report received February 4, 1914, states that she has lost about twenty pounds in weight and that she has become more active sexually. She has taken Armour's desiccated pituitary gland tablets in an irregular and desultory fashion.

The mental hebetude, lack of initiative, psychical depression, and negativism in this case strongly suggested the hebephrenic type of dementia precox. The increased sugar tolerance, osseous changes, physiognomy, and the clinical course spoke for pituitary disorder. It would seem well to bear in mind the possibility of pituitary disease in suspected cases of dementia precox corresponding to the above-described patient. Likewise the class of cases commonly designated as "fat anemics" should be analyzed with a possible pituitary disturbance in view. This condition commonly affects women about the menopause, and is characterized by increased fat, secondary anemia, and the whole train of neurotic

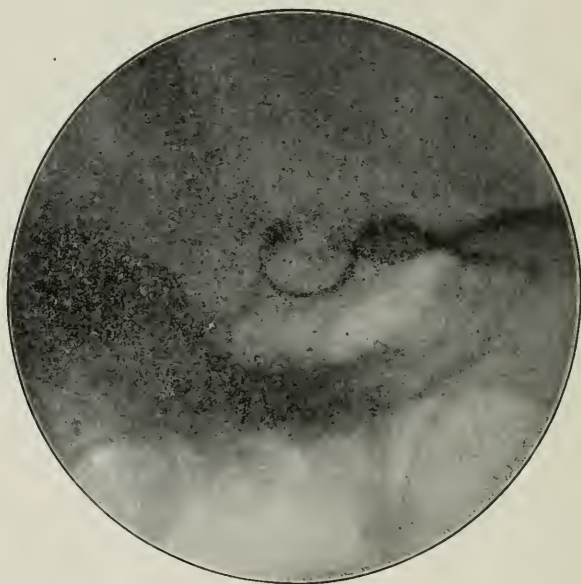


FIG. 4.—Sella measures 10 x 13 mm. The dorsum epiphii appears thickened. Acromegalic symptoms are developing rapidly in this case, although the sella is not markedly changed.

symptoms. The treatment of these cases is highly unsatisfactory, as they react little to the ordinary therapeutic measures. One of these women upon whom operations, rest cure, forced feeding, suggestion, corpus luteum, etc., had been tried, improved markedly on pituitrin. Her sella measured 10 x 13 mm., and her physiognomy strongly suggested acromegaly (this change developed markedly while under observation).

The scope of this paper does not permit of a systematic treatment of the symptomatology of pituitary disorder, and we wish merely to consider briefly the sellar phenomena and certain secretory disturbances.

The roentgenological skull findings in hypophysis disease are manifold and often difficult of interpretation. Sellar enlargement does not necessarily mean *clinical* hypophysis disease, nor does an extremely small sella mean hypopituitarism; therefore much care must be exercised in the interpretation of sellar changes.

The following types may be considered:

1. *Intrasellar growths* widen and deepen the sella so that its floor approaches the floor of the middle fossa. The dorsum epiphii is thinned out, shoved backward, tipped backward, and elongated. Often the posterior clinoid processes partake of the general osseous overgrowth in acromegalics. Changes elsewhere in the skull are often demonstrable—namely, prognathism, large sphenoidal, frontal, and superior maxillary sinuses, thickened skulls, widened sphenoparietal sinuses, digital impressions, and broad sutures with excessive suture indentations.

2. *Extrasellar growths* tend to produce dishing.⁴ The cantel is widened, thinned, and shortened; the floor maintains its normal relation to the base of the skull; acromegalic changes, as a rule, are absent, and there is rather thinning than thickening of the skull.

3. *Large hypophysis tumors* may give rise to complete destruction of the sella, often invade the sphenoidal sinuses, and rarely they may completely destroy the body of the sphenoid. Their extra- or intrasellar origin often cannot be determined at this stage. The anterior clinoid processes may point to their origin, *i. e.*, they are often pushed upward and elongated in intrasellar growths while they are shortened in extrasellar growths.

4. Processes which give rise to increased intracranial pressure will frequently produce changes in the sella. They are more inclined to affect the sella asymmetrically; occasionally basal tumors will distort the sella in such manner that roentgenological differentiation is impossible. Tumors arising in the sphenoid itself may even destroy the surrounding structures and leave the sella more or less intact.⁵

The value of good plates in obscure disorders of growth and of sexual development and activity, and in symptoms pointing to intracranial mischief, can hardly be overestimated. Disturbances of vision, migraine, epileptic attacks, psychical anomalies, trophic disorders—such as obesity, infantilism, impotence, gigantism, dwarfism, menstrual disturbances, without pelvic explanation—should call for an x-ray examination. We have been able to watch the development of pituitary disorder in two epileptics in whom the plates showed sellar deformation. Cushing's case of migraine,

⁴ Schüller, Artur, Roentgen-Diagnostik der Erkrankungen des Kopfes, Wien. u. Leipzig, 1912.

⁵ Schüller, loc. cit.

which was completely relieved by sellar decompression, is worthy of note in this connection.

Recently much evidence has been brought forward to prove the association of diabetes insipidus with pituitary disease. Frank⁶ goes so far as to maintain that all diabetes insipidus is due to posterior lobe hyperactivity. Hypophysectomized animals excrete several times the normal amount of urine in the days following operation.⁷ The same fact has been observed in operated cases. Often glycosuria is present in the first days, to be followed later by an increased sugar tolerance.⁸ This is in keeping with the fact that acromegalics often show decreased sugar tolerance during the developmental stage and later show increased tolerance. Goetsch, Cushing, and Jacobson found in their experiments on carbohydrate metabolism following partial hypophysectomy that there was a transient glycosuria followed by increased carbohydrate tolerance, which could be reduced below the normal by the administration of posterior lobe extracts. A remarkable case has recently been reported by Simmonds⁹ in which a diabetes insipidus followed a carcinomatous metastasis into the pars posterior in which the normal structure was almost entirely destroyed. The pars intermedia and pars anterior were intact. In two cases of diabetes insipidus observed by us the sugar tolerance was high; 450 grams of glucose were given at one time without the appearance of sugar in the urine. The curious fact was observed that *while taking the large amount of sugar the quantity of urine was markedly diminished*. Sellar changes were present in three cases of diabetes insipidus studied, either as enlargement, deformation, or erosion.

The following nosological schema, although not comprehensive, will serve to sketch the conditions resulting from the failure of the pituitary gland to discharge its particular functions in the interlocking glandular directorate which controls metabolism, growth, and sexual life:

1. Affections of the pars anterior:

(a) Hyperfunction—acromegaly, gigantism.

(b) Hypofunction—true or pituitary dwarfism (not chondrodystrophic, rachitic, or cretinic dwarfs).

2. Affections of the pars posterior:

(a) Hyperfunction—diabetes insipidus.

(b) Hypofunction—hypophysial obesity (dystrophia adiposogenitalis).

⁶ Ueber Beziehungen der Hypophyse Zum Diabetes Insipidus, Berl. klin. Woch., 1912, p. 392.

⁷ Crowe, Cushing, Homans, Quart. Jour. Exper. Physiol., vol. ii, pp. 389 to 400.

⁸ Goetsch, Cushing, and Jacobson, Carbohydrate Tolerance and the Posterior Lobe of the Hypophysis Cerebri, Bull. Johns Hopkins Hosp., 1911, vol. xxii, pp. 165 to 190.

⁹ Münch. med. Woch., No. 60, pp. 127 and 128.

3. Mixed affections:

(a) Hyperfunction of the pars anterior with hypofunction of of pars posterior—acromegaly with hypophysial obesity.

(b) Hypofunction of both lobes—dwarfism with hypophysial obesity.

4. Hypophysial disturbance, in conjunction with perverted activity of other glands.

(A) Ovarian or testicular hypofunction with:

I. Hyperfunction of pars anterior—acromegaly with sexual impotence—eunuchoid giants.

II. Hypofunction of the pars anterior—pituitary dwarfism with sexual impotency.

III. Hypofunction of pars posterior—dystrophia adiposogenitalis—genital obesity.

(B) Associated with disturbances in the functions of other ductless glands, *i. e.*, adrenals, pancreas, thyroid, pineal gland, thymus (status thymolymphaticus), etc.

MENTAL MANIFESTATIONS IN TUMORS OF THE BRAIN.

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A REVIEW of the literature concerning mental disturbances in cases of tumor of the brain shows that it is impossible in the light of present knowledge to determine with any degree of accuracy in what particular tumor a certain group of mental manifestations will occur, neither is it possible to draw definite inferences from the seat of the tumor. The literature on this subject is abundant. Classifications have been attempted and tables drawn up to show the frequency of mental disturbances in tumors of various localities of the cerebrum, but a close analysis reveals contradictory statements from equally competent authors.

Some writers believe that in the majority of cases of tumors of the brain disturbances of intellect are observed. They vary from simple intellectual sluggishness to global dementia. The following manifestations are most frequently observed. A stuporous state predominates in the majority of cases. Whether it is exclusively under the influence of the severe pain in the head or it is independent of the latter it is not always easy to interpret. A state of somnolence is quite usual. Indifference and apathy are common. The patient shows lack or loss of interest in surroundings. An intellectual

effort and initiative are frequently in abeyance. In fact, Dupré and Devaux¹ observed in some cases a certain childish mental attitude (*puérilisme psychique*). The patients are infantile in their replies, in the intonation of their voices, in the mimicry; they show impatience and obstinacy characteristic of children in their motives and desires. In contrast with apathy and indolence, not infrequently we meet with undue irritability, emotionality, abulia, outburst of passion and anger. The mnemonic faculties are frequently affected and not rarely from the beginning. The patient cannot recall names and events, and may give the impression of commencing parietic dementia.

The mental disturbances just enumerated do not, as a rule, constitute an embarrassing element in diagnosis of brain tumors, as the other characteristic manifestations of the latter do not fail to make their appearance, such as severe headache, vomiting, vertigo, etc. The difficulty lies in discriminating those cases in which the mental symptoms alone are present for a long time before the physical phenomena develop. Oppenheim and Wallenberg² reported such cases. The diagnosis is also difficult in cases in which the characteristic symptoms of the classical psychoses are present or are predominating in the clinical picture. Melancholia, mania, dementia precox, acute hallucinatory delirium, parietic dementia, all have been diagnosed and postmortem revealed the presence of tumor in the cerebrum.

If we turn our attention to the localization of the tumor and attempt to draw inferences as to a certain relationship between these two factors, we again meet with failure. The presence of a tumor in any region of the brain cannot explain the accompanying psychic disturbances, and the latter cannot therefore be considered pathognomonic of the first. Otherwise speaking a diagnosis of tumor cannot be based on the presence of certain special mental manifestations. Some writers attempted to build clinical pictures special to the frontal lobes, to the corpus callosum, to the temporal lobes, and to other portions of the brain. Thus change of character, such as suspiciousness, hostility, violence, has been attributed to tumors of the frontal lobe. Jastrowitch describes under the name of "moria" and Oppenheim under the name of "Witzelsucht" a jovial and humorous state of mind as characteristic of tumors of the frontal lobe. In diseases of the same region other writers observed various mental phenomena, such as enfeeblement of intellect, depression or childishness (Dupré). Symptoms of parietic dementia have also been observed in tumors of the frontal lobe.

On the other hand, similar identical psychic disorders have been seen also in tumors of the psychomotor zone and even in central tumors. Delusions, hallucinations of all varieties, confusional or

¹ Nouvelle Iconographie de la Salpêtrière, 1901.

² Spezielle Pathologie und Therapie von Nothnagel, Band ix, Th. 1, Abth. 3.

delirious states characteristic of genuine psychosis, may all accompany tumors of the brain. Complete clinical pictures corresponding to the well-established forms of insanity have also been observed in the course of cerebral neoplasms. In one of my unpublished cases a man, aged thirty-five years, presented for months the alternating phases of manic-depressive psychosis. The maniacal periods were particularly long and pronounced. There was not a single somatic symptom indicative of intracranial pressure for a long time, and only three months before he died, papilloedema developed. Patient was operated on and a large tumor was found in the temporosphenoidal lobe of the left hemisphere. In one of my cases which I am about to report the clinical picture for many months was that of parietal dementia, and only shortly before death excruciating headache and vomiting made their appearance. The disease progressed rapidly. At autopsy a tumor was found in the basal ganglia of the left hemisphere.

Among extensive statistical studies of mental symptoms in cerebral tumors those of Shuster and Knapp deserve special mention. The first author in his *Psychische Störungen bei Hirntumoren* reports 775 cases. In 423 cases chiefly mental weakness and dementia were present. In the remaining 352 cases he observed gross mental disturbances suggestive of distinct classical psychoses. The most conspicuous among the latter presented maniacal states (95); the next in proportion were the depressive states (57); then the deliria with hallucinations (52); general paralysis 29 cases and paranoia 19 cases.

In Knapp's tables,³ drawn from a smaller number of cases, we also find clinical pictures of paresis, of delirious, confused, and maniacal states, also of paranoia. Hallucinations are also mentioned. Shuster is apparently inclined to believe in a certain relationship between the type of mental disorder and the seat of the neoplasm, but a close analysis of his records as well as those of other competent observers does not justify any pathognomonic conclusions; neither can any definite relationship be established between the mental disturbances and the nature of the growth.

The pathogenesis of mental manifestations in the course of brain tumors is debatable. The tolerance of the brain for foreign bodies and growths is well known. There are many cases on record showing the presence of voluminous tumors in various areas of the brain without mental disturbances. Multiple tumors have been observed in the same brain without any mental disorder during life. Softening of vast areas in the brain have been observed also without morbid mental symptoms. These facts tend to prove that destruction of one limited area of the brain substance is not sufficient to produce psychic disturbances, that the intellectual

³ Brain, 1906, vol. xxix.

faculties are dependent upon simultaneous coöperation of all constituent portions of the brain. However, mental disturbances have been observed in tumors affecting but limited parts of the brain. Explanations have been sought in various hypotheses. Generalized compression, generalized irritative action caused by localized tumor, auto-intoxication, are the views advanced by various authors for the existence of the mental symptoms. The doctrine of auto-intoxication finds its *raison d'être* in the assumption of continuous absorption of toxic elements originating in the tumor by the venous and lymphatic circulation. The analogy between the clinical picture of uremic encephalopathy and that of cerebral neoplasm is striking. The delirious, hallucinatory symptoms can be readily explained by the toxic pathogenesis. Klippel⁴ believes that we have to deal here not only with an auto-intoxication but also with a secondary infectious process. The latter develops around the tumor and gives place to an inflammation. Not infrequently we find at autopsy an acute inflammation in the close vicinity of the tumor, in the meninges, in the ventricles. Thus headache, convulsions, delirium, fever, coma find their explanation.

Intracranial pressure, generalized irritation, auto-intoxication, and secondary infection may all render considerable assistance in attempts to explain the presence of a great many mental manifestations accompanying cerebral tumors. When, however, we wish to interpret the development of genuine psychoses in the course of brain tumors, the above views fail to give an adequate explanation.

One of the cases here reported presents the most striking resemblance with parietic dementia both from the stand-points of physical and mental manifestations; yet no meningo-encephalitis was found, and a tumor was seen in an area not at all suspected during life. Neither of the above views explains the clinical picture which for a long time remained almost typical of the great psychosis. Only during the last three months signs of intracranial pressure made their appearance. A negative Wassermann reaction both of the blood and cerebrospinal fluid was also one of the most unexpected occurrences, and rendered considerable assistance in making a diagnosis. The second case is one of a tumor of the pituitary body. During life the mental phenomena were of such a nature that the diagnosis of paresis was repeatedly made by competent men. The third case is one of a tumor situated between the frontal lobe and insula in the left hemisphere. During life the patient presented a very marked dulness, apathy, indolence, and extreme somnolence.

CASE I.—C. A. O., aged fifty-six years, contractor of iron works by occupation, drank beer heavily until the last four years of his

⁴ Traité de Médecine de Brouardel and Gilbert, article Tumeurs cérébrales.

life. His family history is unimportant. While travelling in foreign lands twenty years ago he contracted yellow fever and erysipelas, from which he completely recovered. He denied venereal diseases.

Four years ago he developed epileptic seizures. They occurred at first occasionally, but they became quite frequent within the last year. Every week or two weeks he would have an attack, and exceptionally two in the same day. The patient's wife's statements as to the seat of the convulsions were not always the same. Sometimes she thought they were confined to the right side and at another time she would say that she observed them on the left side. Ten months before he died he developed hemiplegia on the right side. The paralysis was at first very slight, but it gradually progressed. Since the onset of the paralysis the wife noticed a gradually oncoming change in the patient's mentality. He became at first listless, inattentive, then he began to be careless about his habits. He would spit on the floor, would not change his underwear for two weeks at a time, would soil his clothes when in the toilet (prior to his present illness he was exceedingly particular about cleanliness and neatness). When reproached he would laugh and agree that he was wrong, but would soon forget it. His memory began to fail about a year ago. Mistakes were noticed in writing letters: he would omit letters and sentences. He began to forget names. He could not recollect voluntarily facts of importance, such as business transactions and money matters. On one occasion he received several checks, and a half-hour later they could not be found. They were recovered the next day in the vestibule of his house on the floor near the hall stand. Shortly afterward the wife noticed a difficulty of expressing himself: his speech became thick and certain letters could not be pronounced clearly.

When he presented himself for examination three months before he died I observed the following conditions: He was distinctly hemiplegic on the right side. His paralysis, however, was not pronounced. The leg was only slightly dragged when he walked. There was no marked rigidity in the arm and leg; nevertheless, the power of both was considerably diminished. The right knee-jerk was increased; there was no ankle-clonus; Babinski and paradoxical reflexes were present on the right. The biceps and triceps reflexes of the right arm were increased when compared with the left side. There was a slight deviation of the face to the right. The pupils were unequal: right larger than left; their contours were irregular. The right pupil reacted somewhat sluggishly to light; both reacted well to accommodation. A slight ptosis was observed on the right side. The right eyeball was somewhat protruded. An ophthalmoscopic examination showed a dilatation of the blood-vessels in both retinæ, but no profound changes in the papillæ. The state of the patient's mentality did not permit to determine whether there was diplopia or not. Ocular palsies were not present,

with the exception of a slight weakness of the left external rectus. The hands and tongue were affected with a fine tremor. There was some ataxia of the upper extremities. The stereognostic sense was preserved in the right hand, but he was unable to name all the objects placed in it. Asymbolia was therefore present for some objects. The general sensibility, objective and subjective, was affected on the right side. Touch, pain, and temperature were markedly diminished on the entire right side, face included. Besides, the patient frequently complained of severe pain in his right arm and leg. Considering the slightness of the motor paralysis, the case so far presented a thalamic symptom-group.

The sphincters were both involved. Involuntary micturition occurred quite frequently. Constipation was obstinate.

The patient's mentality suggested strongly paresis. His facies was drawn; his answers were slow and delayed; the speech was typically paretic, slow with special stoppage on letters *r* and *m*. He looked weak and exhausted, and at the same time he would say, "I feel fine; nothing ails me." He was unable to realize the paradoxical relation between his condition and answers. At times he would clear up and appear brighter, but this improvement would not last long. His memory was decidedly deficient. He was unable to recollect events of two or three days past. He would frequently call his wife by a different name. He could not tell what he ate two or three hours before. Dulness was very conspicuous. When interrogated, he would stare for a while before he would reply, and then the answers were sometimes without any relation to the questions asked.

The condition as just described, including the physical as well as the mental symptoms, suggested strongly the diagnosis of paretic dementia. Soon, however, the clinical picture commenced to change.

He began to complain of severe headache. Formerly he had headache only at the time of an epileptic seizure, but presently it occurred quite frequently and irrespective of attacks. The patient began to have vomiting spells. In the last month they occurred daily and independently of food. His mentality became more and more deeply affected. He had to be fed, he ceased to recognize distinctly his surroundings. The headache became intense, so that he could not sleep; he groaned continuously. The epileptic attacks became very frequent. The hemiplegia became deeper. The vomiting became almost continuous. Finally coma set in and the patient expired after several violent convulsive attacks rapidly succeeding each other.

While under my observation during the last three months of his life the patient was kept in bed with the exception of occasional brief intervals. Thus opportunity was given to study him from every stand-point. Except the liver, which was enlarged, the other

internal organs were found intact. The urine at first contained albumin, which later disappeared entirely. The blood examination as to its physical properties was normal. In view of the clinical evidences of parietic dementia a Wassermann test was made before any treatment was instituted, on the blood-serum and cerebrospinal fluid. To my great surprise the result was negative. A

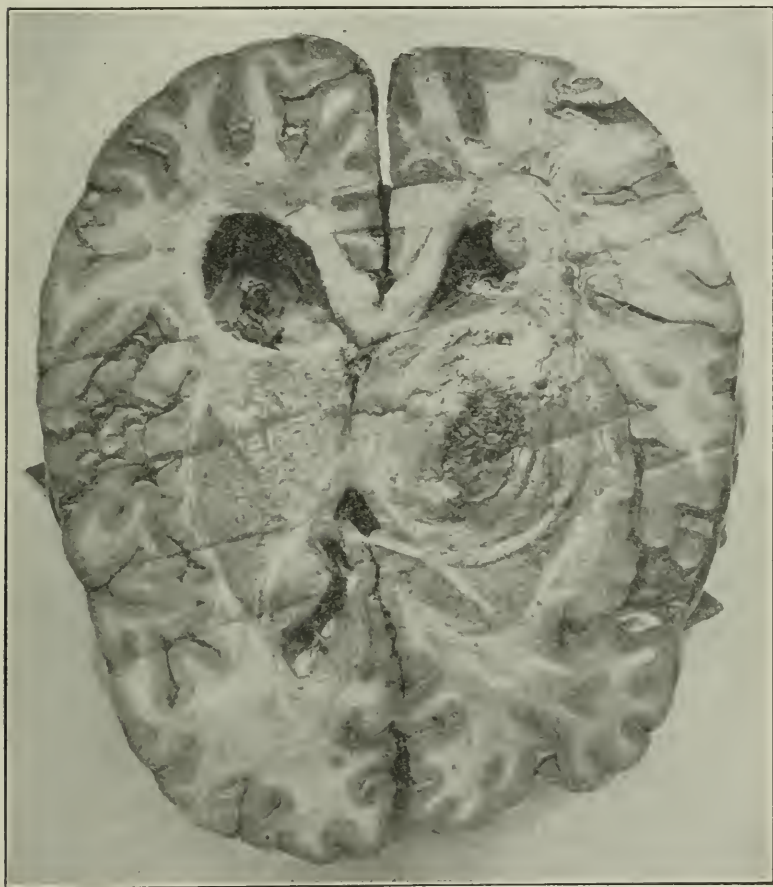


FIG. 1.—Mixed-cell sarcoma in the basal ganglia of left hemisphere.

month later the test was repeated, and again the reaction was negative. The cytological examination of the cerebrospinal fluid showed the presence of a number of lymphocytes and a few polynuclear cells. Each lumbar puncture showed a marked increase of pressure in the subarachnoid cavity, as the cerebrospinal fluid emerged with great force.

The negative Wassermann reaction, in spite of the distinct

clinical symptoms of paresis, made me reject the latter diagnosis. Subsequent events mentioned above proved the case to be one of cerebral neoplasm simulating paretic dementia.

Autopsy performed twenty-four hours after death revealed the following: The heart, lungs, and kidneys were apparently normal. The liver was enlarged and hard. The scalp and skull were of normal thickness, and presented no abnormalities. The dura was pale and the vessels were bloodless. A noticeable feature of the dura was its thickness and resistance to cutting. On the left side, in front of the anterior end of the longitudinal fissure, the brain protruded in spots through the dura. This area, of the size of about a square inch, resembled a leaf which was moth-eaten; the dura covering this area was extremely thin.

The brain was remarkably dry, and there was little fluid after its removal. A tumor was found at the base of the left hemisphere of about the size of an almond. It resembled a convolution which had been pushed out from above downward and from behind to the left of the pons (Fig. 1).

The cord was apparently normal. A transverse anteroposterior section of the brain revealed a large tumor within the basal ganglia of the left hemisphere, destroying the largest part of the caudate and lenticular nuclei, also the adjacent part of the optic thalamus, pushing backward, forward, and externally the neighboring tissues. The tumor extended downward to the base, where it appeared on the side of the pons covered by the cortical substance. Histologically the tumor presented a mixed-celled sarcoma. Below the tumor the tracts were in a state of degeneration.

CASE II.—H. S., aged thirty-one years, a watchmaker, was apparently well until the age of twenty-three. At that time the following symptoms developed gradually: ptosis of the left upper eyelid; diplopia; diminution of visual acuity of the left eye; vertigo; headache. The mental phenomena consisted of frequent attacks of loss of consciousness followed by a confusional state lasting two to three weeks at the time. The patient also showed a fine intention tremor of the hands and of the tongue. This condition lasted five years, during which the diagnosis of paretic dementia was made by several competent men.

At that time he began to develop the following symptoms: Bitemporal hemianopsia, optic atrophy in the left eye and optic neuritis in the right eye. Further examination revealed strikingly infantile genitalia and lack of sexual desire. Soon a descending right hemiplegia made its appearance. The patient began to increase in weight; he became markedly adipose, so that six months before he died he weighed 235 pounds. He became enormous. The attacks of unconsciousness continued, and they were followed by prolonged confusional states as before. The adiposity, the bitemporal hemianopsia, with increasing blindness, the infantile genitalia—all

finally suggested an angiosarcoma of the pituitary body which was verified by autopsy (Fig. 2). For a long time the case presented the picture of paresis until the characteristic eye symptoms and the adiposity began to make their appearance.⁵

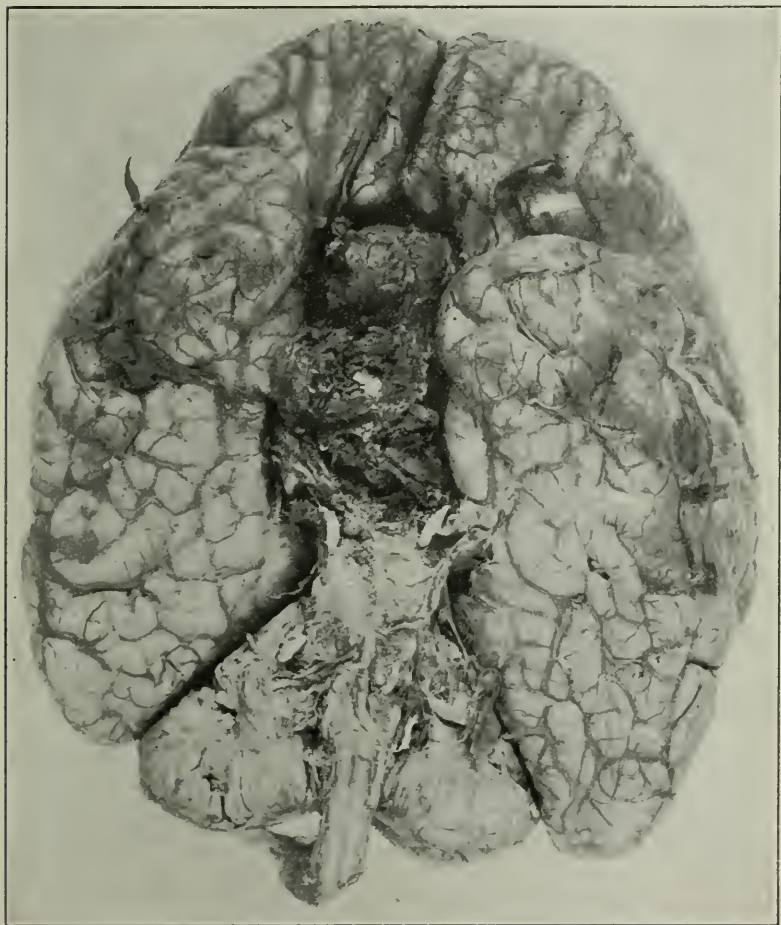


FIG. 2.—Tumor of pituitary body (angiosarcoma).

CASE III.—An Italian boy, aged sixteen years, presented for a long time headache, gradual loss of sight, ataxic gait, loss of knee-jerks, and Achilles tendon reflexes on both sides, with Babinski on one side and paradoxical sign on both sides. The eyes soon showed a high degree of papillitis. The patient's speech was slow. Mentally he presented a marked dulness, apathy, and indifference

⁵ Jour. Amer. Med. Assoc., 1912, lix, 171.

to surroundings. An operation failed to relieve him (Fig. 3). At autopsy a large round-celled sarcoma was found wedged in between the frontal lobe and the insula of the left hemisphere.⁶

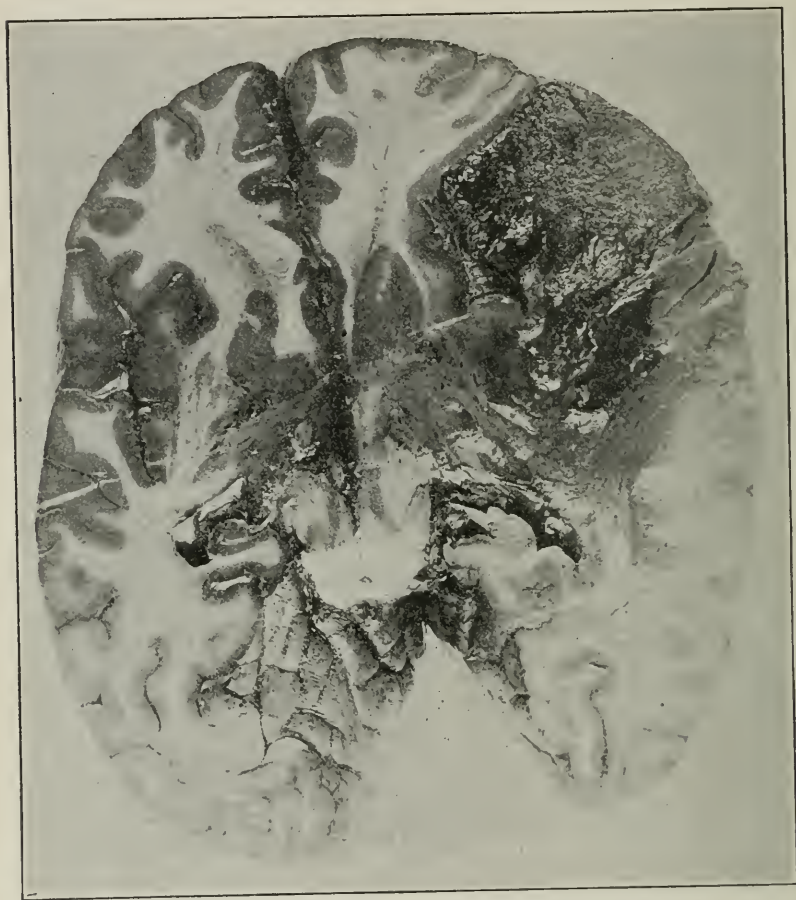


FIG. 3.—Tumor (round-cell sarcoma) wedged in between the left frontal and temporal lobes, penetrating the lateral ventricle.

While the frontal lobe of the left hemisphere suffered considerable compression, nevertheless the mental manifestations consisted only of mental dulness and indifference. We have seen above the tendency of some writers to lay especial stress on the frontal lobe and to find especially grave symptoms which could be considered as pathognomonic of an involvement of this particular portion of the brain. This case speaks emphatically against such a view.

⁶ New York Med. Jour., January, 1913.

PERIPHERAL PIGMENTATION OF THE CORNEÆ, ASSOCIATED WITH SYMPTOMS SIMULATING MULTIPLE SCLEROSIS.

BY T. B. HOLLOWAY, M.D.,

PHILADELPHIA.

IN 1902 Kayser referred to a peripheral annular pigmentation of each cornea in a patient whose nervous symptoms seemed to warrant a diagnosis of multiple sclerosis, and in the further course of the disease diabetes and pigmentation of the skin developed. Since the first report by Kayser, the histories of several other cases showing analogous ocular and nervous manifestations have been recorded. Recently the condition has been especially studied and discussed by Fleischer.

The clinical findings in the patient whose history is recorded below warrants the inclusion of this case in this particular group.

Mc G., aged twenty-seven years, was admitted to the University Hospital on the service of Drs. Charles K. Mills and William G. Spiller, December 12, 1912,¹ complaining of loss of control of his arms and voice.

History of Present Condition. The patient stated that he was perfectly well until the latter part of March, 1910, at which time he noted that the right hand would tremble and shake when he attempted to write. When writing it was necessary for him to steady the right hand with the left, and in a few months he was compelled to give up this method and do his writing with his left hand. In July, 1911, his voice became somewhat affected, so that he talked, as he expressed it, as "one who is afraid to speak." On December 25, 1911, he first became aware that the left hand was becoming affected in the same manner as the right. From that time on the tremor increased in extent and severity, until at the present time he is not able to button his clothes, brush his hair, or feed himself. This tremor disappears when he is quiet or after he has been in bed for a few minutes. In the summer of 1912 he first noticed that his head would start to shake, especially when he would talk. This also has increased in the past few months. For the past year there has been a jumping sensation in the muscles of his legs, as if they were contracting suddenly, but he has felt no loss of power, pain, or loss of control. This only occurs when he is lying in bed or sitting still, never when walking. Otherwise

¹ This patient was first seen by me late in the summer of 1912, through the courtesy of Dr. A. C. Sautter. He was then under treatment at the German Hospital, and had been referred to the service of Dr. W. T. Shoemaker, for ocular examination, where he came under the observation of Dr. Sautter. He was exhibited at the April, 1913, meeting of the Philadelphia Neurological Society.

the patient feels perfectly well; he has not lost in weight; sleeps well; in fact, is rather drowsy all the time. He never has headache, but has some dizziness when rising from bed or from a stooping position. His appetite is good; his bowels, as a rule, are regular, but for the last month he has been somewhat constipated. There are no cardiac or respiratory symptoms.

Previous Medical History. He has had the usual diseases of childhood. Since a boy he has been subject to vague rheumatic pains in the left arm and leg. No other sickness except gonorrhea a number of years ago, which persisted for one year. He denies syphilis. He never sustained any injuries and never had any traumatic or inflammatory ocular condition.

Social History. He has been a painter for the last fourteen years, but has seldom used white lead, and none in recent years, his work calling for varnish. Mostly all of his work has been done in the open. He has used tobacco to excess. Since the summer of 1912 he has drunk very little, but prior to that he averaged seven or eight glasses of beer a day.

Family History. Negative. No history of nervous, cardiac, renal, or lung trouble.

Physical Examination. The patient is a large-framed individual, with good musculature; well nourished; no stigmas of hereditary taint. The face presents a distinctly dusky appearance, but the scalp is not affected. There is a suggestion of a fine capillarity over the cheeks and nose. On both legs over the anterior and outer surfaces there are large areas of brownish-yellow pigmentation, occurring in blotches. He thinks this has been present for about ten years. There are no evidences of edema. The skin is soft and moist. The peripheral arteries are not sclerosed. The pulse is slow and full and of fair tension.

Nervous System. The gait is normal. Station is good. There is a questionable tendency to Romberg's sign. The patellar, biceps, and triceps reflexes are somewhat exaggerated, but equal on the two sides. No ankle clonus; no Babinski sign. No change in the abdominal or cremasteric reflexes. There is no disturbance of sensation; the muscular power of the arms and legs is good. The tongue when protruded is not deviated to either side, but is accompanied by a slight tremor. The seventh nerve is intact. Speech is rather syllabic, slow, and deliberate. Heel-to-toe test is negative. Finger-to-nose test shows marked intention tremor. There is no propulsion or retropulsion. No dysphagia.

General System. The ears are apparently normal; the throat is negative; the teeth are poor; there is no blue line. The lungs, heart, liver, spleen, and abdomen are negative.

Ocular Examination. There is no true nystagmus, but at the extreme limits of the lateral rotations a faint nystagmoid jerk can be noted. The ocular rotations are not impaired. The pupils

are larger than the average, but react promptly and normally to the various reflexes. By oblique illumination an annular pigmented zone can be noted about the periphery of the cornea of each eye, which produces a distinct contrast in color between the covered and exposed portions of the blue iris. With a Zeiss loupe there can be noted an annular pigmentation of the cornea which apparently involves the deepest layers. In the right eye this pigmented area is widest above and to the nasal side, and narrowest below and to the temporal side. The width of the involved area varies from 2 to $3\frac{1}{2}$ mm. At the more peripheral portions it presents a smoky or brownish appearance, which fades into a brownish-green as the pigment disappears in the more central uninvolved portions of the cornea. The apparently clear central portion of the cornea is oval. With a Nernst lamp and a Zeiss corneal microscope there is a suggestion of a finely granular appearance toward the limbus, but this is not pronounced. The cornea is not vascularized, nor does it show any opacities that might be the result of congenital or inflammatory conditions. No pathological changes could be seen in the iris. With the ophthalmoscope no opacities were seen in the lens or vitreous. The disks were nearly round, suggestive of a reddish-gray type, but no pallor of the temporal sector was seen; no evidences of neuritis. There were no vascular changes, and the choroid and retina were healthy. The fields for form and colors were normal, and no scotoma could be elicited either by the ordinary perimetric examination or by Bjerrum's method.

O. D. = .50 pp. 13.5 cm., with + .25 cyl. ax. $180 = \frac{6}{5} +$.

O. S. = .50 pp. 13.5 cm., with + .25 cyl. ax. $165 = \frac{6}{5} +$.

Progress of the Case.—December 16, 1912. Urine: cloudy and straw colored; sp. gr., 1011; alkaline; faint trace of albumin; sugar negative; bile, urobilin, and indican negative; casts, mucus, and red-blood corpuscles negative; occasional white corpuscles; amorphous phosphates and urates.

Blood. Red corpuscles, 4,330,000; white corpuscles, 7100; hemoglobin, 75 per cent.; polynuclear, 65; lymphocytes, 28; transitional, 2; eosinophiles, 5.

Blood Pressure. Systolic, 125; diastolic, 80.

Levulose Test. December 19: 65 grams of levulose in 200 c.c. of water were given on a fasting stomach and the urine collected every hour for five hours. Except for the third-hour test, which was spoiled, a positive reaction was obtained for each examination. (Dr. F. G. Sproul.)

Wassermann Test. Negative.

December 21. Examination by Dr. O. H. P. Pepper confirmed the above findings, but owing to several punctate bluish granules at the gum margin an examination for degeneration of the red cells was suggested. A slight cervical adenopathy was noted.

Feces. Light brown, semisolid; no fat or mucus; occult blood negative; slight trace of bile; plant cells, muscle fibres, epithelium, leukocytes, bacteria, yeasts, crystals, and debris.

Blood examination for basic degeneration was negative.

December 23. Stomach contents: specimen a creamy, turbid fluid, with granular sediment and brown specks. Free HCl, 60 per cent. (dimethylamidobenzol); total acid, 75 per cent.; lactic acid, 0; occult blood, negative; starch, yeast, bacteria, leukocytes, Oppler-Boas were negative.

February 6, 1913. Levulose test by Dr. J. Gordon Saxon: With 40 grams of levulose a typical reaction to resorcin was obtained for six hours; this was confirmed by spectroscopic examination. With 30 grams of levulose there was a similar result.

March 16. A test for increased sympathetic tonus was made by Dr. Arthur Hopkins and gave a positive result. A hypodermic injection of ten minims of adrenalin (1 to 1000) was given and the case observed during the following hours. The blood-pressure was raised 18 points; marked tremor provoked; sugar tolerance markedly reduced and lymphocytes increase by 13 per cent.

A Röntgenogram of the head by Dr. H. K. Pancoast was negative.

May 4. Hemoglobin, 70 per cent.; red-blood cells, 4,050,000; white-blood cells, 7000.

During the several months the patient was under observation there was an improvement in his tremor, but aside from this there was practically no change. The station and gait remained normal, and no psychic phenomena developed. Drs. Hartzell and Knowles, who examined the skin lesions, reported a colloid degeneration of the skin of the forehead and a mild type of acne rosacea associated with a pigmentation of the legs, due to blood pigment, which occasionally follows erythematous eczema.

In 1910,² in an article on corneal pigmentation, I had occasion to casually refer to this particular type of pigmentation, but at that time I had never observed a case, and had overlooked a contribution to this subject by Fleischer in 1909.³ This observer has especially studied the few cases of this character that have been observed or at least recorded, and has had opportunities to study the two cases that have come to autopsy, so frequent references will be made to his findings. Since I could find references to but five cases that exhibited this type of corneal pigmentation it may be well to review these histories.

In 1902 Kayser⁴ reported from the Tübingen Clinic the history of a male, aged twenty-eight years, who for five years had what was regarded as multiple sclerosis. While the patient was not regarded as a confirmed alcoholic, the first symptoms developed after alcoholic excesses. In each eye there existed an annular

² *Annals Ophthalm.*, 1910, xix, 685.

³ *Münch. med. Woch.*, 1909, p. 1121.

⁴ *Klin. Monatsbl. f. Augenheilk.*, 1902, xl, ii, 22.

peripheral pigmentation of the cornea, which began at the limbus and gradually faded away centrally, so that a central oval area of the cornea remained normal. The widest part of the pigmentation was above and below, more in the former position. Examination with the Zeiss microscope did not reveal any abnormalities at the limbus or in the cornea itself, other than the pigmentation, which was dense enough to obscure the iris. The peripheral portion was noted to be made up of an accumulation of yellowish granules, which became finer and more diffuse centrally where the color changed to yellowish-green. This pigmentation was observed to be deep; the superficial and middle layers of the cornea were not affected. Fleischer had further opportunities to study this patient, and has reported on the later findings.⁵ The patient was intermittently under observation up to the time of his death in May, 1909. During this period the nervous phenomena became worse, distinct psychic phenomena occurred, while late in the course of the disease there developed diabetes and a grayish-brown pigmentation of the head and hands, with grayish discoloration over the chest and abdomen. The liver was palpable, but not the spleen. There was no reduction in the visual acuity, but the pigmentation of the cornea increased, and there was some lessening of the light sense.

Autopsy. The liver was rather small and nodular, the spleen enlarged, and the kidneys pigmented. There was a small localized patch of thickened pia near the vertex. Macroscopically and microscopically there were no signs of multiple sclerosis. Microscopically the cornea showed a pigmentation of Descemet's membrane that extended centrally about 1.9 mm. The deposit consisted of rounded and angular greenish-brown granules that appeared refractile at a certain angle. This deposit was separated by a clear space from the endothelial cells, which were normal in appearance. The only other structure of the eye that presented any pigmentation was the hyaline membrane of the choroid or the membrane of Bruch. Here the deposit was more marked than in Descemet's membrane, and the granules finer than in the adjacent pigment epithelium and the pigment cells of the choroid. The interstices and fibres of the eye muscles were pigmented, as was the optic sheath, but the nerve itself was free. In the kidneys the basement membrane of the urinary tubules were especially pigmented. In the liver the pigment was found in the interstitial connective tissue. There were evidences of degeneration of the liver cells and proliferation of the connective tissue. The spleen was markedly pigmented, especially in the trabeculae and walls of the bloodvessels, and also in the pulp, but here it was mostly extracellular. In the intestines the pigment was present in the

⁵ Bericht der Ophthalmologischen Gesellschaft, Heidelberg, 1908, p. 128.

vessel walls and in the circular muscle. The connective tissue of the heart was pigmented, while in the skin the basal layer of epithelium was affected, also the connective tissue of the hair follicles and the basement membrane of the sweat glands. The pia was pigmented, but the lungs were free. The adrenals were normal. The condition of the pancreas was not described.

In the following year Fleischer⁶ at the same clinic observed two similar cases. This first patient was a male, aged twenty-nine years, with a kyphosis. Venereal disease was denied and there was no history of alcoholism. The patient had a high hyperopia, congenital amblyopia, and horizontal nystagmus. Nervous symptoms in the form of an intention tremor first appeared a year before. This patient had the same type corneal pigmentation as above described. His neurological condition was regarded as pseudo-sclerosis. The patient later developed distinct psychic changes and an intermittent glycosuria. He died in February, 1906.

Autopsy. The consistency of the liver was increased, its surface nodular, and on section, increase of the connective tissue was noted. There were evidences of slight chronic emphysema and bronchitis. The cardiac muscle showed some degeneration, the left ventricle was hypertrophied and the aorta and coronary arteries were atheromatous. The spleen was enlarged. In the stomach there was a copious hemorrhage and the scar of a cicatrized ulcer. In the brain the lateral ventricles were dilated, there were evidences of a chronic external pachymeningitis and chronic leptomeningitis, but discolored sclerotic patches or focal brain lesions were not found. No mention was made of the condition of the adrenals or pancreas, and no microscopic examination was made.

The second case was a male, aged thirty-one years. The left eye had been enucleated, owing to severe corneal ulceration secondary to dacryocystitis, but unfortunately no microscopic examination had been made. The right eye presented the type of corneal pigmentation now under discussion. Nervous symptoms had existed for two or three years, and were attributed to multiple sclerosis.

The fourth case was observed by Salus.⁷ The patient was a male, aged thirty-two years, who had been affected with nervous symptoms for a number of years. When seen in February, 1908, there was noted an annular brownish-green pigmentation of the corneæ, which presented a granular appearance when studied with the Zeiss microscope. The neurological condition was regarded as multiple sclerosis.

At the conclusion of Fleischer's⁸ most recent article he has briefly referred to a fifth case that has been observed by Gallus,

⁶ Klin. Monatsbl. f. Augenheilk., 1903, xli, p. 489.

⁷ Medizinische Klinik, 1908, iv, 495.

⁸ Deutsch. Zeitsch. f. Nervenheilk., 1912, xlv, 179.

as well as Westphal.⁹ This patient was a girl, aged nineteen years, who had greenish discoloration of the corneæ and a tremor resembling that seen in pseudosclerosis, but up to the time of his report no discoloration of the skin or diabetes had developed.

Among the patients so far affected all have been young adults, and five of the six patients were males. Several of the case histories make reference to preceding rheumatic affections or pains in the extremities and in one case there existed prolonged gastric disturbance some time prior to the onset of the disease. In Kayser's case the symptoms first developed after alcoholic excesses; Salus' patient attributed his to exposure to cold. No probable cause could be found for the other cases. The fact that the patient whose history is above recorded was a painter seems to be significant, but he used lead but little in his work, and not at all for the past few years; there was no history of colic and no basic degeneration of the red cells. He was, however, a consistent beer-drinker, and in the use of varnishes would be exposed to methyl alcohol; however, there is no history or ocular indications of any acute intoxication from this latter substance, but the possibility of some influence brought about by the frequent use and handling of this substance cannot, of course, be denied. The most conspicuous symptom and the one that has been constant in all the cases has been the marked coarse intention tremor affecting the arms and head in all cases, and in some the lower extremities as well. In Fleischer's first case and in the one here recorded the gait was normal, but in the others it became rather spastic. In all of the cases the cranial nerves were normal. Fleischer in speaking of Kayser's case states that the speech was not scanning in type, but owing to the tremor it was difficult; in the patient whose history is here recorded the speech was certainly affected more than could be accounted for by the tremor alone, and further no change was noted when the patient was quiet. Kayser's and Fleischer's first patient were the only ones to develop psychic phenomena, and in each instance this change was pronounced. The knee-jerks were exaggerated in Kayser's and Fleischer's second case, as well as in the case above mentioned, but in Fleischer's first case they were normal. In Salus' case they were absent. Ankle clonus was intermittently present in Kayser's case; Salus does not refer to it; while in the other cases it was absent. The abdominal and cremasteric reflexes were absent in Salus' case and were affected late in Kayser's case; in the other cases no change was observed. Salus does not refer to Babinski's sign, but in the other cases it was absent. In Kayser's case the head and hands presented a grayish-brown pigmentation of the skin, while there was some grayish discoloration over the

⁹ Since forwarding this manuscript to the editor, I have found reference to a recent article by Westphal (*Archiv f. Psychiatrie und Nervenkrankheiten*, 1913, li, Heft 1), but at the present writing the original is not available.

chest and abdomen. While I did not find any reference to skin pigmentation in the history of Salus' case, Fleischer states a brownish pigmentation of the head was observed. The condition of the face and legs in the case here recorded has been referred to above. Glycosuria has been observed twice, and in a third case, while there was no glycosuria, there did exist a decided reduction in the sugar tolerance.

All of these cases showed the same type of cornea pigmentation. A deep annular pigmentation beginning at the limbus, appearing brownish green in color, and in its denser peripheral portion presenting a "smoky" appearance. It can readily be overlooked, and in brown irides would be especially difficult to detect, even by a trained observer. It is also well masked by a mydriatic, owing to the retraction of the iris behind the pigmented area. Its true character can only be detected with a loupe. Aside from the pigmentation it can be said that in all cases the eyes were negative, and did not show the changes so frequently present in cases of true multiple sclerosis. The vision remained unaffected.

In the two cases that have come to autopsy there existed a cirrhosis of the liver, associated with splenic enlargement and other changes already alluded to.

REMARKS. The diverse and complex character of the symptoms exhibited by the patients who have shown this type of corneal pigmentation makes the study of this group of cases most interesting. Kayser at the time of his report regarded the pigmentation of the cornea as congenital. Fleischer in the following year, while he called attention to the association of the corneal condition with symptoms of multiple sclerosis, was doubtful of their direct connection, although he did not exclude the possibilities of the pigmentation being an acquired condition. In a later brief reference¹⁰ to it he stated that he believed it to be in some way connected with the debilitated condition of the patients. Salus believed the neurological condition to be multiple sclerosis, and suggested that Fleischer's case, regarded as pseudosclerosis, was also one of multiple sclerosis, and he believed there was an undoubted connection between the corneal pigmentation and the nervous symptoms. He called attention to the fact that the pigmentation most closely resembled blood-staining of the cornea, and based his suggestion on the work of Lapinski in reference to degeneration of the vessels in lesions of the sympathetic, he thought it possible that owing to innervation disturbances in the canal of Schlemm there resulted a slow filtration from this canal and imbibition of the coloring matter of the blood by the deeper layers of the cornea. While the incomplete autopsy on Fleischer's case in 1906 gave some suggestion of the complex character of some or possibly all of these

¹⁰ Klin. Monatsbl. f. Augenheilk., 1908, xlvii, 91.

cases, it was not until opportunities were offered for more careful study in the case first observed by Kayser that a pigmentation of the internal organs was definitely demonstrated. Fleischer has made a most painstaking study of this case, and in his recent able contribution has discussed the various phases of the conditions presented.

Since in both of the cases that came to autopsy there had existed a glycosuria, with the postmortem findings of cirrhosis of the liver and enlarged spleen, associated with marked widespread pigmentation of the internal organs in the one case, and in the other (Fleischer's) the macroscopic examination intimate the possibility of analogous pigmentation, the possibility of a hemochromatosis or bronzed diabetes was immediately suggested.

The pathogenesis of hemochromatosis is still obscure. Probably the most prevailing opinion is that the pigmentation is the primary condition; Letulle¹¹ has regarded the diabetes as the original factor, while Potter and Milne¹² state that "it would seem as if today we are warranted in stating only that cirrhosis of the liver is the primary condition; that the hemochromatosis, always in slight degree in liver cirrhosis, is in some cases very excessive, and causes a general pigmentation which eventually also involves the skin; and finally, that the whole process is not any definite symptom-complex, but a chain of circumstances which rarely seems to be completed." On the other hand, Sprunt,¹³ supporting the opinion of Opie,¹⁴ regards it as a distinct morbid entity, and states there is no evidence of any abnormal blood destruction. He considers it a metabolic disease, "manifested, especially, by a change in the chromogenic groups of the proteid molecule with the deposition of pigments, and believes that the fibrosis of the various organs is dependent upon pigmentary degeneration and the accumulation of pigment in the interstitial tissue.

In the case so thoroughly studied by Fleischer, instead of finding the iron-containing hemosiderin and the iron-free hemofuscin, which characterize cases of hemochromatosis, he found a pigment that did not give the usual reactions of these pigments, and its exact character has not been definitely determined, although he believes the pigment to be a blood derivative. For the exact chemical properties of the pigment found, the reader is referred to Fleischer's recent article. Owing to the conflicting reports concerning the character of the pigment present in this case, its careful study has added but little if any to our meager knowledge concerning the physiological and pathological body pigmentations.

While this group of cases has certain symptoms in common with those found in hemochromatosis, reference to some of the more

¹¹ Cited by Potter and Milne.

¹² AMER. JOUR. MED. SCI., January, 1912.

¹³ Archives of Internal Medicine, 1911, viii, p. 75.

¹⁴ Trans. Assoc. Amer. Phys., 1899, xlv, 253.

convenient articles bearing on the latter subject, such as those contributed by Opie, Blumer,¹⁵ Potter and Milne, and Sprunt, failed to reveal any reference to cases associated with nervous phenomena such as characterized these cases, and no reference is made to any corneal pigmentation that has been observed; on the other hand, Fleischer shows that the ocular microscopic findings are quite different.

This same observer also considered the possibility of poisoning by various metals especially silver, and pointed out certain resemblances to cases of manganese poisoning. As to the latter substance, this can be definitely excluded in the case here recorded, by the history, and I dare say the same is true about the other cases in this group. Casamajor¹⁶ has recently referred to 9 cases of possible manganese poisoning, and has reviewed the literature. In the one case of his series that came to autopsy a superficial inspection of the brain-stem blocks before embedding, suggested the possibility of slight changes about the lenticular nucleus.

As to silver, while a chemical examination of small pieces of the kidney and spleen in Fleischer's case seemed to show the presence of this metal, certain other tests seemed to make this improbable, and it was further pointed out that there was no history of the patient having taken silver; that in argyrosis no such nervous and psychic symptoms develop, nor is the pia pigmented. It was also stated that the cornea is never involved in argyrosis. While this may be the case after argyrosis produced by the ingestion of silver, Knies¹⁷ has referred to a brownish pigmentation of the cornea after cauterizations with silver nitrate stick. In this case the corneal epithelium and endothelium were not involved, but the stroma, Bowman's membrane and Descemet's membrane, were pigmented, as were the large deep lymph spaces and the four straight eye muscles.

In the case studied by Fleischer, the pigment, so far as the eye was concerned, seemed to have a selective action affecting two of the three important hyaline membranes of the eye, the membranes of Bruch and Descemet, both of which contain elastic fibres. The exemption of the lens capsule was explained by him as due to difference in chemical properties.

Fleischer has also considered pseudosclerosis and diffuse cerebral sclerosis. Oppenheim¹⁸ and Potts and Spiller¹⁹ refer to the difficulties attending the diagnosis of pseudosclerosis, while Wilson is still more emphatic and thinks the term should be abandoned.

Volsch²⁰ has placed on record the history of a case that he believed

¹⁵ Yale Med. Jour., 1912, xviii, 190.

¹⁶ Jour. Amer. Med. Assoc., 1913, lx, 647.

¹⁷ Klin. Monatsbl. f. Augenheilk., 1880, xviii, 165 (cited by Parsons, The Pathology of the Eye) Jahresbericht f. Ophthal., 1880, 194.

¹⁸ Text-book of Nervous Diseases, translated by Alexander Bruce.

¹⁹ Jour. Amer. Med. Assoc., 1905, xlv, 1455.

²⁰ Deutsch. Zeitsch. f. Nervenheilk., 1911, xlii, 317.

to be analogous to Fleischer's, and has seen fit to group these with certain other cases attributed to pseudosclerosis. In his case there was also a cirrhosis of the liver, but no pigmentation of the cornea or internal organs. While corneal pigmentation was not especially sought for, he thinks it unlikely that this could have been overlooked. Wilson,²¹ in an admirable monograph, has recently called attention to a definite syndrome occurring in the course of progressive lenticular degeneration, which he describes as "a disease which occurs in young people, which is often familial, but not congenital or hereditary; it is essentially and chiefly a disease of the extrapyramidal motor system, and is characterized by involuntary movements, usually of the nature of tremor, dysarthria, dysphagia, muscular weakness, spasticity, and contractures with progressive emaciation; with these may be associated emotionalism and certain symptoms of a mental nature. It is progressive and, after a longer or shorter period, fatal. Pathologically it is characterized predominantly by bilateral degeneration of the lenticular nucleus, and in addition cirrhosis of the liver is constantly found, the latter morbid condition rarely if ever giving rise to symptoms during the life of the patient." In the four personal observations of the author careful ocular examinations were evidently made, in the other case histories reviewed by him, eight in all, the ocular reports were incomplete or wanting, but in no case was there any reference to a pigmentation of the cornea, and the eyes were normal in other respects as well. All of the cases that came to autopsy had a marked cirrhosis of the liver, but nowhere in his careful and elaborate reports does he refer to any pigmentation of the internal organs. Wilson thinks that in connection with the hepatic cirrhosis, which does not produce any clinical signs during the life of the patient, a toxin is probably generated which exerts a selective action on the cells and fibres of the lenticular nucleus. In the addendum he alludes to Volsch's case, and believes it belongs in the group of cases he has so carefully described. He also refers to Fleischer's case, but makes no positive statement in regard to it, although the inference is that he would similarly classify it.

In the patient whose history is here reported the essential signs and symptoms have been the tremor, the character of the speech, and the corneal pigmentation. While no glycosuria manifested itself, there existed a marked reduction in the sugar tolerance. As above noted, the skin lesion of the face was attributed to acne rosacea, while the yellowish-brown pigmentation of the legs was said to be due to blood pigment such as at times follows erythematous eczema.

It is at least interesting to note the marked positive reaction this patient gave to the test for increased sympathetic tonus, the

²¹ Brain, 1912, xxxiv, 295.

tremor being most markedly exaggerated for a period of two days. In this country Barker²² and Hopkins²³ have referred in detail to the vagotonic and sympathicotonic states, and I am much indebted to the latter observer for his interest in the present case. While our present knowledge of the so-called autonomic and sympathetic systems may not warrant our drawing any definite conclusion, the results are none the less interesting, especially in cases of this character where the pathogenesis is obscure and unknown.

With the uncertain results in the chemical and microchemical tests in the case studied by Fleischer, considering the opinion expressed by Wilson, and the absence of pigmentation in the cases studied by him, as well as in the case referred to by Volsch, one may well ask whether we are really dealing with an acquired pigmentation of the cornea that has any connection with the other symptoms noted in these cases?

Concerning this it may be pointed out that in the 6 cases that have shown corneal changes the pigmentation has been bilateral; the cornea and the intra-ocular structures have been free from evidences of any traumatic or inflammatory condition apt to be associated with corneal pigmentation. But excluding a high refractive error and squint that were present in one case, other defects or anomalies that might be regarded as congenital have been wanting, unless, despite two autopsy reports, we regard the neurological symptoms as dependent upon a true multiple sclerosis, and accept the views of Strümpell, Ziegler, and Müller²⁴ that this affection is due to a congenital tendency to proliferation of the glial tissue. While all of the cases except one (Salus) exhibited this type of pigmentation when they first came under observation, all of them had been otherwise affected for a year or more. None of these cases had conical cornea, and, at any rate, there is practically no resemblance between this and the superficial annular pigmentation described by Fleischer and Hudson²⁵ as having been observed in cases of keratoconus. In one case (Kayser's) the pigmentation was said to have increased while the patient was under observation. To the best of my knowledge corneal changes of this character have not been observed or at least recorded except in association with the symptoms noted in these patients. Even if one accepts the report of the presence of silver (kidney and spleen) in Fleischer's case and eliminates the possibility of an associated pigment, it is hardly reasonable to suppose that all six of these cases had argyrosis.

²² Trans. Assoc. Amer. Phys., 1912.

²³ Preliminary report read before the Section of Medicine, College of Physicians of Philadelphia, February, 1913.

²⁴ Cited by Oppenheim, Text-book of Nervous Diseases, translation by Alexander Bruce, vol. i, p. 333.

²⁵ Royal London Ophthalmic Hospital Reports, 1911, xviii, 198.

In the absence of more definite data concerning the character of the pigment it is futile to speculate as to the manner in which the eye structures become affected; at any rate, the study of cases of true hemochromatosis has still left the question of the formation and possible transposition of the pigment an open one. Since the publication of Wilson's observations and deductions, cases of this character will be watched with additional interest, and in turn it is hoped that in the study of certain clinical conditions already mentioned, the possibility of corneal pigmentation will be borne in mind.

From the study of these cases we can only conclude that in association with certain symptoms, of which a coarse intention tremor affecting the extremities and head is the most conspicuous, there may develop a deeply seated annular brownish-green pigmentation of the cornea. That some or possibly all of these cases are associated with a cirrhosis of the liver, which has been shown to exist in 2 cases. That during the course of the disease a glycosuria or a lowering of the sugar tolerance may develop. Accepting the autopsy findings in 2 cases and the neurological opinions expressed on the case whose history is here reported, the nervous manifestations are not due to multiple sclerosis.²⁶

In conclusion, I gratefully acknowledge the courtesty extended by Drs. Mills, Spiller, and de Schweinitz for placing this patient at my disposal for clinical observation.

INFANTILISM.

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THE name infantilism was coined by Lasègue, who designated by it the persistence of childish characteristics, physically as well as psychically, into adult life. With the increasing knowledge of various clinical pictures the term underwent modifications, having been circumscribed by different authors in varying ways. A great impetus was given to the studies of the various forms of retarded and checked development by the investigations of the functions

²⁶ Since this manuscript was forwarded to the editor, Rumpel (*Deutsch. Zeitsch. Nervenheilkunde*, 1913, xlix, Heft 1 u. 2, S. 54) has referred in detail to the character of the liver changes and the pigmentation. He believes the hepatic changes depend upon a faulty fetal development which results in a functional insufficiency that gives rise to disturbances of metabolism and auto-intoxication, and that this is responsible for the neurological symptoms. The pigmentation he regards as an argyrosis.

of the endocrine glands, which proved their great influence upon the physical and psychical growth. In connection with these studies, only the names of Hegar, W. A. Freund, Halban, Di Gaspero, and Anton may be here mentioned.

At present a general and a partial infantilism is recognized; yet a definite determination of infantilism against a number of other pathological conditions is at present not always possible. The term is not yet precise, and the various attempts at making subdivisions of this anomaly are not free from objections. Anton, with an attempt at an etiologic arrangement, gives a table of the various forms of infantilism, which in its modification by Dietrich is as follows:

1. Infantilism without detectable causes (genuine infantilism, primary defectiveness of the germinal cell).

2. Infantilism due to disturbance of inner secretions.

(a) Infantilism with myxedema and cretinism (thyreogenic).

(b) Infantilism with absence or underdevelopment of the genitals (dysgenitalism).

(c) Infantilism due to disturbance of the various visceral glands, as thymus, parathyroid, suprarenals, pancreas, etc.

3. Infantilism due to other internal disturbances.

(a) Infantilism in primary brain diseases.

(b) Infantilism in angioplasia.

4. Infantilism due to toxic and trophic disturbances.

(a) By intoxications of the parents (alcohol, lead, mercury, etc.).

(b) By congenital lues.

(c) By extra-uterine diseases, as f. i. intestinal catarrh, tuberculosis, valvular disease, pellagra, malaria.

5. Mongolism, Anton.

General infantilism, according to Anton's definition, is a disturbance of the development, characterized by a persistence of infantile or childish characteristics in the whole organism, preventing the development of the individual to the full extent of his species; not only the physical characteristics of childhood persist, but generally the psychical qualities also.

The principal features enumerated by most authors are: smallness, retarded or arrested growth of the skeleton and musculature, and corresponding smallness of all organs; underdevelopment or lack of the sexual organs, with that of the secondary sexual characters; finally the persistence of the psychic functions in the infantile or childhood stage.

However, we encounter various morphological as well as etiologic types of general infantilism, and in various degrees, varying from only slight development to the highest degrees of dwarfism. Infantilism is a morphological anachronism. When applied to the

early life, the term has only a relative meaning, of course, designating the persistence of size and characteristics of an earlier age.

Partial infantilism signifies the persistence of the infantile state in one organ or organ system or in the psychic functions. In the strict sense, also, general infantilism is only partial, inasmuch as there is perhaps never a complete congruence in the organs, their functions, the proportions of the parts, the psychic functions and the metabolism with those of infancy or childhood. A valuable contribution to the subject of partial infantilism was published by Tandler of Vienna in the *St. Paul Med. Jour.*, 1908.

DYSTHYREOGENIC INFANTILISM. The type of general infantilism, to which attention was first directed, is the dysthyreogenic form, as we meet this frequently and most markedly as myxedema and cretinism. While the clinical picture of grave congenital or early acquired myxidiocy as an expression of athyreosis is familiar, it is equally important in view of the success of the organotherapy, to pay attention to the clinically abortive forms of myxidiocy, that are due to only a partial interference with the function of the thyroid gland, the hypothyroidism. Hertoghe pointed out the fact that between the "myxedème franc" (athyreosis) and the functional integrity of the thyroid there exist various degrees, some of which may be compatible with the intellectual requirements of ordinary life. To these forms he applied the term "hypothyroïdie benigne chronique" or "myxedème fruste." We meet here all gradations from marked cretinoid habitus to the slight, hardly recognizable disturbances, which occasionally can be ascertained only *ex juvantibus*.

The "formes frustes" may present the cardinal symptoms of myxidiocy—namely, myxedema, dwarfism, and psychical disturbances—though in a milder degree and without imposing the stigma of physical and psychical degeneracy upon the afflicted.

They appear as individuals of more or less infantile exterior. Their habitus and size correspond to about the proportions of the newborn, in that they have a relatively larger head, round, fleshy face (full-moon face), a nose more or less saddled, and a stunted body. The navel may be low and the genitals are small and underdeveloped. The subcutaneous tissue is not firm, but doughy and flabby, although it seems at first sight similar to that of the infant; the skin is dry and scaly and the perspiration absent or scanty. The radiogram shows delayed ossification; the metabolism is subnormal. In the incomplete forms the face is expressionless, but less stolid than the extremely idiotic expression in athyreosis.

The intelligence is, as it seems, always affected, though occasionally only to a small extent; the apperceptive and thinking processes being heavy, slow, and clumsy. This is also seen in the inefficient or mediocre progress in school. However, the patients may learn reading, writing, and arithmetic, and may pass the elementary

school even with fair results in exceptional cases, as did, for instance, the two patients of Siegert. This would be impossible in athyreosis.

Even when there are only slight disturbances of the intellect, in the affective sphere they be more pronounced, inasmuch as the patients are rather apathetic, indifferent, and emotionless, as the monotony of the expression also demonstrates. Their muscular actions are slow and clumsy, as for instance, walking. Typical cases have been described and illustrated by Jannin, Magnus-Levy, Mennaches, Marfan and Guinon, Siegert, and others.

Siegert's interesting case concerned an eleven-year-old boy. There was myxedema with dwarfism, but a degree of mental development, incompatible with the complete picture of myxidioey. He had passed even the entrance examination for the "Sexta" (High School in Germany). The correctness of this diagnosis was also confirmed by the splendid success of the specific therapy.

The following case is equally typical, and is remarkable for the splendid result of the organotherapy. This patient has been under my observation since January 17, 1911:

Emma F., of Norwood Park, a suburb of Chicago, (Fig. 1), born September 30, 1898. Parents, Germans, are farmers, healthy; no dwarfism, goitre, nor cretinism in the family. Breast-fed for fourteen months. The child learned to walk at eighteen months. Until the age of two years she was of normal size. She had obstinate constipation from the first, was always quiet and somewhat clumsy, and slow in her motions. She spoke rarely, but no other peculiarity was observed in her speech. The mother remembers that the child perspired around the nose in the summer. The child was always sensitive to cold and chilly, therefore she would crouch near the stove. Even in warm weather her hands and feet were cool, and looked bluish and marbled. She lacked the inclination to play and frolic around like other children, and is still awkward in dressing herself without help. At the age of six and one-half years she entered the public school, where she passed in reading and writing, with rather good results, but was poor in arithmetic. She learned little poems and prayers in the Sunday School without much trouble. When eleven years old her dentition corresponded to that of a child five years younger, according to the statement of a dentist. Her appetite had always been poor. The girl is at present in the fifth grade.

Status Præsens. January 17, 1911 (Fig. 1). Girl, aged twelve years and four months. Body length, $43\frac{1}{4}$ inches (instead of $58\frac{1}{2}$); weight, 53 pounds (instead of 88 pounds). Head big, face round (full-moon face), somewhat puffy, and with a monotonous, cretinoid, "worried" expression. The nose is saddled and the forehead wrinkled; there are swellings of the subcutaneous tissue on the chin and in the region of the forehead, especially of the glabella and above the eyebrows.

The teeth are incomplete, many of them being absent. The tongue is not enlarged.

The integument in general is pale and dry, and on the arms, legs, and the lower parts of the trunk it is rough.

There are moderate swellings of the subcutaneous tissue above the clavicles, over the pectoralis muscle, in the lower part of the abdomen and more markedly on the mons Veneris. The hands and feet are cool, with their dorsal surfaces distinctly puffy, and the skin of the arms and legs is marbled (*cutis marmorata*). The thyroid gland is not palpable. The abdomen is protruding; there is no umbilical hernia. The intelligence corresponds to the anamnestic data.



FIG. 1.—Hypothyreogenic infantilism before thyroid treatment.



FIG. 2.—Same case as Fig. 1, after thyroid treatment.

Diagnosis. *Forme fruste* of myxidiocy (hypothyreogenic infantilism, type Brissaud).

The diagnosis was confirmed by the remarkable effect of the thyroid therapy. I saw the child repeatedly and the gradual changes were easily seen.

April 17, 1911. The child measured $45\frac{1}{2}$ inches in height (an increase of $2\frac{1}{4}$ inches in three months), although the body weight was one pound less than before treatment.

January 7, 1912. The length was 49 inches (an increase of $5\frac{3}{4}$ inches in one year).

April 30, 1912. Length, $50\frac{1}{4}$ inches.

August 3, 1912. Crines pubis are appearing on the labia majora.

September 30, 1912. Patient grew the last month $\frac{3}{4}$ inch; measures 52 inches; this means a total growth of $8\frac{3}{4}$ inches within nineteen months.

She is a healthy-looking, red-cheeked girl, and helps assiduously in the daily housework. The arms and legs have still a tendency to be cool and marbled, and the child is still sensitive to cold. The excellent effect of the thyroid therapy, which was periodically interrupted, was evident by the pronounced acceleration of the growth, which surpassed the normal ratio within this period of time, by the disappearance of the subcutaneous swellings, by the more intelligent expression of the face, by the eruption of many teeth, and by the improvement of the psychical backwardness, in the disappearance of the torpor, which was replaced by normal quickness. The abdomen became less prominent, the defecation regular. How much the type was changed after three years' treatment with thyroid is well demonstrated in Fig. 2.

DYSGENITAL INFANTILISM. As is well known, a disturbance of glands other than the thyroid may also retard normal mental and psychic growth. Numerous researches into the function of inner secretion prove the importance of harmonious correlation and equilibrium among the various endocrine glands for the normal development of the whole organism and its parts.

Thus one series of cases of infantilism originates from a disturbance of the sexual glands. They exert an important influence upon the organism, to a certain extent even before puberty, as the common experience of stock breeders shows. The normal growth, the sexual impulses and potency, and the full development of the secondary sexual characters depend upon the functional integrity of the interstitial tissue, that is, the Leydig cells of the testicle and the corresponding cells of the ovary.

Tandler and Gross, for instance, observed in male deers the development of rudimentary antlers (*Perückengeweih*) only after castration, but not after the experimental destruction by x-rays of the generative part of the testicles, thus leaving the inner secretory interstitial cells unaffected.

Castration in young boys doubtless is rare, but the testicles may be completely destroyed by congenital luetic processes (castratio subalbuginea, Scringe) that are identical in their effect. Observations on man could be made profitably among the various people who practise castration, for example, the Skopzes in Russia or the eunuchs in the Orient.

The type of infantilism caused by a defective function of the sexual glands is termed dysgenitalism. The patients thus afflicted may be called eunuchoids, a term coined by Tandler and Gross in Vienna on account of their resemblance to the eunuchs. Other

terms used in the literature are infantilism avec gigantism, dys-trophia adiposogenitalis, gero-derma genitodystrophico.

The dysgenitalism may present itself in two differing principal types: gigantism and adiposity, although transitional forms exist.

In the dysgenital giants of the first group we meet the following features: the period of growth extends beyond the normal time, occasionally even beyond thirty years of age. This abnormal increase of length affects especially the lower extremities, resulting in the characteristic "eunuchoid" longleggedness. The epiphyseal cartilages remain unossified beyond the normal limit of time, in some cases even beyond the age of thirty years, which condition can be demonstrated clinically by the x-rays. The genital organs are only slightly or not at all developed, and the secondary characters are absent or only suggested.

These types, that is, gigantism and dysgenital adiposity, are both encountered among eunuchs and also among the Skopzes in Russia. Tandler, in a number of cases, found an enlargement of the hypophysis cerebri, the sella turcica in the x-ray picture being enlarged and deepened. This enlargement of the hypophysis together, with the genua valga, found in dysgenital gigantism as well as in acromegaly, has led Brissaud, Meige, and others to assume a certain relationship between gigantism and acromegaly. In fact, giants have been observed in whom later acromegaly supervened.

The abnormal persistence of the epiphyseal cartilages is considered a consequence of inhibition of the inner secretion of the sexual glands, and this condition is necessary, of course, for an increase in length, which will result where hyperactivity of the hypophysis is present. When the epiphyses are ossified the result of hyperactivity of the hypophysis will be acromegalic growth only.

In dysgenital adiposity the second clinical form of dysgenitalism, a lack of development of the sexual organs and the secondary sexual characters is likewise present. The larynx remains small and cartilaginous even late in life. There exist also longleggedness, though less pronounced, and a retarded ossification of the epiphyseal cartilages and genua valga. The pelvis resembles that of a child or a castrate. The chief difference between this condition and gigantism is the presence of abnormal adipose tissue, occasionally increased to a marked degree, and in special localizations that are characteristic of genital origin. The mammary regions especially have deposits of abundant adipose tissue to such a extent that they may take on the appearance of female breasts. Furthermore, exaggerated deposits of panniculus adiposus are located in the regions of the hips and ad nates in the lower region of the abdomen, and on the mons Veneris, which may be separated from the suprapubic fat by a deep furrow, as in children. A high-pitched voice and beardless face complete the picture of feminism.

The face is sallow, the skin soon becomes wrinkled and senile, therefore this affection is named also *geroderma*. Tandler and Gross found that the thymus persisted an abnormally long time in many cases. The *x*-ray examination showed the hypophysis cerebri was usually not enlarged.

The connection between the above-described characteristic type of adiposity and disturbances of the germinative glands is experimentally established as a fact by castration of animals and man. In addition to this, we find in castrates and in eunuchoids very early a penetration of fat tissue into the musculature as in castrated animals.

It must be remembered, however, that this whole problem is rather more complicated than it seems at first sight, being entangled by numerous phenomena due to the correlation and simultaneous functional disturbances of other glands of internal secretion. I only point here to the fact, that, although increased length is the rule among the eunuchoids and Skopzes, in some individuals only normal, subnormal, and even small measurements are observed. Eunuchs and eunuchoids, although similar, are by no means identical, and data by experimental castration should be only applied with great caution in explaining eunuchoidism, in which the sexual underdevelopment may be only a part of a general abnormality. It is not yet explained, also, why in one case primary dysgenitalism leads to gigantism, in the other case to adiposity. Tandler and Gross reported only male eunuchoids; female eunuchoids have been reported lately by Peritz, Wolff, and Hutchinson.

PITUITARY EUNUCHISM. A clinical type of adiposity, similar to that in dysgenitalism, is also found accompanying pathological processes of the hypophysis cerebri, in the so-called hypophyseal adiposity or pituitary eunuchism.

Since Froehlich, who in a case of tumor of the hypophysis observed adiposity and underdevelopment of the sexual glands in addition to the tumor symptoms, has emphasized the diagnostic importance of the first symptoms in hypophyseal affections, this type has been repeatedly seen and verified by postmortem or during operations (v. Eiselsberg, Frankl Hochwart). When it develops in boys or youths the external sexual organs remain in an immature state, the perigenital hairs are scanty and have boundaries of the feminine type, the beard is absent, the skin is delicate and hairless, and the voice is high-pitched—in short, the secondary sexual characters are not normal. In addition to this, adiposity is a prominent feature, striking by its eunuchoid localizations more than by its degree, thus giving the individual an appearance of feminism like in eunuchs and dysgenital eunuchoids. In most cases the size of the body remains below the average; also dwarfism has been observed. These facts deserve special attention in respect to the relationship between hypophysis and growth of

body. The symptoms are of course less pronounced, when starting after maturity.

Many varieties, deviating in various degrees from this classic type do occur, but without completely obliterating the original. Hypofunction of the pituitary gland (hypopituitarism) is responsible—possibly directly, according to the views of some authors, or indirectly according to others, as Schüller and Tandler, etc., who maintain that the dystrophic adiposity take place only when the disturbance of the hypophyseal function entails a disturbance of the germinative glands, that is, Leydig's cells.

Although in pituitary adiposity mostly lesions of the hypophysis (tumors) are to be found, in a number of cases no palpable anatomical lesions of the hypophysis were present. Many other problems of this complex subject being unsolvable as yet, the question arises whether we have to deal in such cases with a primary eunuchoidism or secondary eunuchoidism, in which the pituitary gland, although apparently anatomically normal, may functionally be deficient, thus exerting a detrimental influence upon the development and function of Leydig's cells.

Endogenic adiposity of enormous degrees has been observed in childhood as early as in the first two years of life. While we may ascribe it to hypothyroidism, accepting the views of Hertogh, who regards it as an attenuated form of infantile myxedema, we also have to acknowledge in some instances of adiposity in children hypopituitarism as the causative factor since the studies of Frankl Hochwart, Froehlich, Madelung, Marburg, and others. But perhaps it is the insufficiency of the inner secretion of the germinative glands—an imperfect or delayed formation of Leydig's interstitial substance—which is more often responsible for adiposity during the age of prepuberty, in boys especially, who show the eunuchoid localizations of the adipose tissue. This adiposity may be either only temporary or permanent.

After these considerations we will outline here the history of the following case, that will lead to a further discussion as to the possible pathogenesis (Figs. 3 and 4).

Wilhelm M., of Chicago, aged twenty-one years, one month; parentage, German. Family history, negative. As a child he developed in an entirely normal way mentally and physically. A photograph taken when he was five years old corroborates this statement of his parents. He was entirely healthy until about eight years old, when he suffered from typhoid fever, accompanied by delirious states; this kept him in bed for about two months.

A remarkable retardation of his longitudinal growth dates from this time. This was accompanied by a gradual, slow increase of the adipose tissue that attained a striking degree. For the following six years he suffered from cephalalgia, which was at first only slight, but later intense and almost daily.

A photograph of the boy in his fourteenth year, with a group of his classmates, demonstrates by comparison the pronounced change, to wit, alteration in the body form, the striking shortness, and adiposity. Crines pubis since about four years. No libido; coitus and masturbation denied; during the last year pollutiones nocturnæ at long intervals; erections rare. Patient asserts that his perspiration is scanty even after exertions, and that he is easily chilled in cool weather. The intelligence is good.

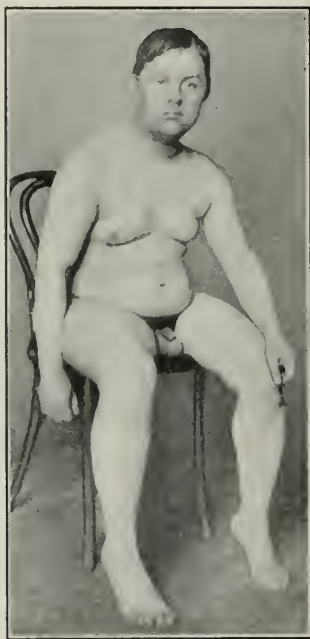


FIG. 3.—Eunuchoid localizations of adipose tissue.



FIG. 4.—Dorsal view of Fig. 3.

I saw the boy the first time on September 25, 1911. The status præsens was the following: Patient was aged twenty-one years, two months; $57\frac{7}{8}$ inches high, the size of a normal thirteen-year-old boy. Weight, 133 pounds (average weight of a thirteen-year-old boy is 84.67 pounds). A much increased flabby panniculus adiposus, with special localizations of predilection, as in the mammary regions, that have a more or less feminine form (as seen in Fig. 3), above the clavicles, under the chin (double chin), on the abdomen especially in its lower part; therefore it is prominent; on the upper arms, thighs, hips, ad nates, and on the mons Veneris, which is separated from the abdominal adiposity by a furrow, somewhat

as in a child. These eunuchoid localizations, together with the broad hips and slanting shoulder lines, give the man a body type similar to the female, even if seen from behind as Fig. 4 demonstrates. The head is big and the face full, but with an immature, infantile expression. There is only the slightest suggestion of a beard or mustache. The axillary hairs and crines pubis are well developed, the latter, however, being of the feminine type in their boundary. The larynx is small and without projecting thyroid cartilage. The voice is high-pitched, so that, when talking over the telephone, he is often mistaken for a little boy or girl, as the patient himself admits. The hands are small, graceful and feminine. The *x*-ray picture of the hand shows the epiphyseal cartilages of the phalanges and metacarpals not yet ossified. The sella turcica in the *x*-ray picture of the head seems to be of normal shape and size. It is impossible to palpate the thyroid on account of the adipose tissue.

Genital Organs. Penis short, somewhat smaller than normal, and deeply buried under the cushion of the adipose tissue of the mons Veneris; the scrotum is of normal size, the testicles also of about normal size, but drawn high up within the scrotum; the prostate gland is small.

Intelligence and memory are good; patient is musical, good-natured; but immature in his character.

MEASUREMENTS OF THE BODY.

Body height	57 $\frac{3}{4}$ inches
Circumference of the head	22 "
Breadth of the shoulders	16 "
Stretch of arms	58 $\frac{1}{2}$ "
Circumference of the chest at the level of the mamæ	36 "
Circumference of the abdomen in the level of the epigastrium	32 "
Circumference of the abdomen in the level of the umbilicus (umbilicus is low, only 2 inches above the horizontal line of the cristæ ossis ilei)	37 $\frac{1}{2}$ "
Distance of the umbilicus from the processus xiphoideus	8 $\frac{1}{2}$ to 9 "
Distance of the umbilicus from the symphysis	5 $\frac{1}{2}$ "
Distance of the symphysis from the floor	28 "
Circumference of the thigh at the level of the perineum	22 "
Circumference of the upper arm	12 $\frac{1}{2}$ "
Distance of the cristæ ossis ilei	10 $\frac{1}{3}$ "

There is no doubt that in this case a disturbance of inner secretion, due probably to typhoid infection, is the underlying cause. This is evident from the small size of the patient, the eunuchoid adiposity, the non-ossification of the epiphyseal cartilages at the age of more than twenty-one years, certain anomalies in the sexual sphere form the lack of the normal development of certain secondary characters, accompanied by a certain degree of immaturity of character.

The scanty perspiration, chilliness, and universality of the adiposity would suggest a participation of the thyroid. However, the failure of the thyroid therapy to influence these conditions

militates against this assumption. On the other hand, disturbances of the function of the skin are known to exist in affections of the hypophysis, as hyperhydrosis in acromegaly and scanty perspiration in hypopituitarism.

Progressive obesity has been observed not infrequently after typhoid, due to its deleterious effect upon the thyroid. Von Noorden mentions two such cases and quotes another, where a strumitis during typhoid was followed by obesity and a few years later by myxedema. We encounter several similar instances in the French literature. But in a number of cases the adiposity after infections was due to an involvement of the pituitary gland by meningeal processes, as they are observed in pneumonia, scarlatina, typhoid, etc. Indeed, my case offers some features that Neurath observed in one of the cases, that he described and illustrated under the title "Fettkinder" (obese children). That case was the following:

Boy, aged ten years; after scarlatina, when seven years old, there developed an enormous, monstrous adiposity; the growth was remarkably retarded and the boy suffered from attacks of headache and vertigo. The boy's size, 109 cm., corresponded to the size of a normal boy of six years of age, while his weight was 36.8 kilos, corresponding to the body weight of a thirteen-year-old boy. Circumference of the head, 53 cm. The testicles were well developed; the penis was hidden in the adipose tissue of the mons Veneris. The x-ray examination of the skull demonstrated signs of hydrocephalus to some degree, but a normal sella turcica. Neurath asserts an affection of the hypophysis in this and similar cases, caused by a hydrocephalic effusion due either to meningitis serosa accompanying scarlatina or to a small tumor that could not be detected by the x-rays.

In analogous cases, as for instance those reported by Marinesco and Goldstein, Babonncix and Paiseau, Krueckmann and Meyer, and Kurt Goldstein, the pathogenic factor was a pressure lesion, with consequent hypofunction of the hypophysis through hydrocephalic effusion that distended the third ventricle, calling forth symptom pictures of pituitary adiposity.

It is an interesting and important fact that extirpation of the hypophysis in animals has resulted in adiposity, resembling degeneration adiposogenitalis in man (Cushing, Aschner).

Retardation and cessation of growth, caused by hypofunction of the pituitary gland, is known by clinical observation as well as by animal experiments. Among others, Babinski found in a seventeen-year-old girl a tumor of the hypophysis as the sole explanation of the syndrome of infantilism, and Benda reports a case of pronounced dwarfism combined with a complete destruction of the hypophysis by a tumor, consisting of hyaline tissue, osseous trabeculae, epithelial cells, and cholesteatoma masses.

Among the patients of Marinesco and Goldstein, Kurt Gold-

stein, Babonneix and Paiseau, some are of a strikingly small size and have large heads. In one of the cases of Babonneix and Paiseau the morbid adiposity started after scarlatina, as in the case reported by Neurath. We may infer from these various reports that this type of pituitary adiposity in children may occur with or without a clinically demonstrable disturbance of the genital organs (dysgenitalism). Biedel, among 32 cases of hypophysary adiposity, found only twelve with genital atrophy, and states that in the beginning of the affection a genital involution cannot always be found.

In the light of the above observations the case described by me possibly may be classified under the category of cases of pituitary adiposity as exemplified by the case of Neurath above quoted.

The intense headaches since the typhoid would argue in favor of a possible meningitis serosa during his disease, though unfortunately no more exact data than the vague statement that the patient was for some time delirious could be had as to the course of the typhoid. The lower reflexes are not increased. Among other points the lack of longleggedness speaks against a primary (partial) dysgenitalism. The symptoms in the sexual sphere with the underdevelopment of some of the secondary sexual characters then would be secondary, induced by a disturbance of the hypophysis.

PLURIGLANDULAR INFANTILISM. In myxedematous infantilism the athyreosis is the principal but not exclusive factor, the function of other endocrine glands being more or less involved. Atrophy of the genitals, atrophy, interstitial inflammation and abnormal persistence of the thymus (Sainton and Rathery), hypertrophy (L. Meyer Aschoff), atrophy with cystic degeneration (Pontif) of the hypophysis cerebri, and atrophy of the adrenals have been observed. In fact, according to the views of Sante de Sanctis, the whole system of the endocrine glands is involved.

Gougéro and Claude devoted careful studies to the subject of "insufficance pluriglandulaire endocrinienne." By this term is understood the symptom-complex of insufficiency of a number of endocrine glands, as of the thyroid, testicles or ovaries, adrenals, hypophysis, etc.

As the associations of pluriglandular insufficiency are various and of different degrees, it is plain that there does not exist only one syndrome but a series of syndromes, varying according to the glands affected, the degree and succession of the disturbance of each single gland, and the age of the person.

Claude and Gougéro bring the history of an instructive case of pluriglandular insufficiency concerning a forty-nine-year-old man.

An alcoholic, with chronic tuberculosis of the lungs and lymph-glands. During convalescence from acute nephritis there appeared symptoms that rendered the case interesting, namely loss of the genital functions, loss of the secondary sexual characters, as loss

of beard, axillary hairs, pubes, change of the voice; atrophy of the testicles and the penis; a syndrome indicating insufficiency of the sexual glands; chilliness, dryness, and desquamation of the skin; an old, wrinkled face; atrophy of the thyroid; psychological decline; emaciation; asthenia; in the last months pigmentations of the skin and a striking decrease of the arterial pressure, which was interpreted as suprarenal insufficiency. The insufficiency of the thyroid, testicles and suprarenals, recognized during life, was verified by autopsy and histology, which in addition revealed lesions of the hypophysis, pancreas, parathyroid, kidneys and liver.

The authors collected from the literature a number of similar cases, described under various names, as those of Rumpel, Dalchè, Sainton and Duprè, Brissaud and Bauer, Gandy, etc.

In the young, pluriglandular insufficiency must needs result finally in infantilism, since the three glands which control the growth, namely, thyroid, sexual glands, and hypophysis, are involved.

A transitional case from primary dysgenitalism to pluriglandular insufficiency is reported by Peritz; interesting cases of pluriglandular infantilism were reported by Richon and Jeandelize, by Peritz, Nazari, Campioni, and others. In Nazari's case there were present infantilism, tuberculosis of the lungs and meninges, a cystic degeneration of the hypophysis, persistence of the thymus, hypoplasia of the thyroid and testicles.

As yet the clinical differentiation of pluriglandular infantilism from Lorain's type might be occasionally impossible, and perhaps by further studies some of the groups of Lorain's type will have to be classified among the groups of pluriglandular infantilism.

DYSTROPHIC INFANTILISM. The type Lorain differs morphologically and etiologically from the type of Brissaud, exemplified by the first case of my series. Lorain described in 1871 the dystrophic type of infantilism, named after him. The individuals affected by it are small but graceful in contradistinction to Brissaud's hypothyrogenic type; they have "elegant, fine" forms; the extremities are long, the abdomen is not prominent, the adipose tissue not increased; the contours of musculature and skeleton are therefore not masked. It is true the genital organs are small, but they may be proportionate to the body. The intelligence is mediocre, small, childish, like the body. This type resembles *un homme miniature*, and presents, as Meige tersely says, the picture of a normal individual, seen through the opera-glass reversed. The aspect, therefore is that of one approaching puberty rather than that of an infant. The following case is an example (Fig. 5).

Charles H., of Chicago. Parents and two sisters healthy; no dwarfism; no lues; no alcoholism; nor abortus. The patient is the first child, born, allegedly, six to seven weeks before full term. Mother, then aged twenty-seven years, suffered from repeated attacks of acute rheumatic polyarthritis during the pregnancy.

At birth the boy was small and puny; the physician estimated the weight as 2 pounds, evidently an underestimate. Eyebrows and nails at birth were absent or hardly visible. For eight weeks the baby was kept wrapped in cotton near the stove, in order to be saved. Breast-fed for thirteen months, though always dyspeptic and diarrheic during this time. First teeth at the end of the first year; at sixteen months his weight was only $10\frac{1}{2}$ pounds; at this time he learned to talk. He walked when twenty-two months old. At two years he was so small that he was demonstrated before an audience of physicians in St. Luke's Hospital as a curiosum. Afterward he was always sickly: he had chicken-pox, whooping cough, with a hernia as a sequela, existing for two years, severe scarlatina, and repeatedly bronchitis. At eight years he entered school, where he was backward. During the last two years he made mentally and physically comparatively great progress. However, at present he is only in the third grade of the public school, although twelve years and four months old. Thyroid therapy for five months, three years ago, had no effect whatsoever.

Status Præsens. August 11, 1912. Boy, aged twelve years four months. Size, $50\frac{1}{2}$ inches (normal for this age, 55.4 inches). Weight, 42 pounds (normal, 76.9 pounds). Thus this boy is the size of a normal nine-and-one-half-year-old boy, while the weight is that of a five-and-one-half-year-old boy. The child has a healthy look and small, graceful stature. The skeleton is delicate and the musculature and panniculus adiposus is poorly developed. The skin is delicate, smooth, and moist, with a good, healthy, and abundant growth of hair on the scalp. No swelling of lymph glands. The head is markedly dolichocephalic (cephalic index, 67.8). The face is long and narrow. The teeth are normal and in good condition. Internal organs normal. Diastasis of the musculi recti abdominis. The medial lobe of the thyroid distinctly palpable; the lateral lobes not with certainty. Crines pubis limited to around the root of the penis; the right testicle is small, of the size of a bean, 1 cm. long, instead of olive sized for this age. The left testicle is slightly smaller than the right one, and is retained in the inguinal canal, but can be drawn into the scrotum. The penis is only $1\frac{1}{4}$ inches long, with the glans broad and thick. The mental development is backward, perhaps about as much as the physical.

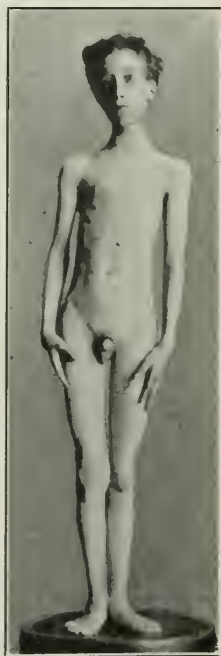


Fig. 5.—Lorain's type.

MEASUREMENTS OF THE BODY.

Height	50½ inches
Head: Circumference	18⅝ "
Bitemporal diameter	3½ "
Biparietal diameter	4½ "
Frontoöccipital diameter	6⅔ "
Mentoöccipital diameter	8 "
Circumference of the chest at rest in mammary line (normal 24¾ inches)	21 "
Breadth of shoulders	10½ "
Stretch of arms	48½ "
Distance of the symphysis from the floor	26 "
Distance of the cristæ ossis ilei	7½ "
Circumference of the abdomen in umbilical line	18½ "

The following case deserves to be mentioned here because its prenatal history is similar to that of the foregoing case:

Mamie B., the second among four children, born at full term. Mother suffered during this pregnancy from severe rheumatic polyarthritis, which kept her in bed for almost eight months. The girl was at birth very small, weighing, by report, only one and a half pounds; breast-fed for one and a half years, with the addition of other food after the first year. First teeth at eight months; learned to walk at one year and three months and to talk in the third year. She has always been healthy, but suffered last year for some time from enuresis nocturna.

Status Præsens. Girl, aged six years nine months, healthy looking, but very small. Body weight, 29½ pounds (weight of a normal girl two years old). Height of body, 39⅝ inches (size of a normal girl two and a half years old). Circumference of chest only twenty inches. Fronto-occipital circumference of head, twenty inches. Distance of symphysis from floor, 19⅔ inches. Body graceful, well proportioned, panniculus adiposus and musculature poorly developed. Teeth complete, in very good condition. Skin smooth, of healthy color, so also the mucous linings. Abdomen somewhat prominent. Urine normal.

Though the morphological type of Lorain is unmistakable and characteristic in its pure form and differing from Brissaud's type with its more or less infantile somatic attributes, yet occasionally it may in forms not well marked be difficult to differentiate them clinically in the young. In such cases the anamnesis and thyroid therapy will be helpful, Brissaud's dysthyreogenic type showing a rapid and decided improvement.

It is not surprising that combinations of both types occur, since the etiologic factors causing dystrophia may be complicated by hypothyroidism, as in the interesting case of Duprè and Pagniez.

ETIOLOGY. In the etiology of dystrophic infantilism, factors which call forth a debility of the whole organism come into consideration. This form is encountered sometimes accompanying the status lymphaticus and as a consequence of chronic infections;

above all, either in lues hereditaria or in lues acquired very early; in descendants of parents who are suffering from tuberculosis, chronic alcoholism, pellagra, malaria, leprosy, or other endemic diseases; in persons with congenital or early acquired valvular disease, particularly with mitral stenosis (nanisme mitral) or pulmonary stenosis. It is found also in individuals showing only malnutrition and poor unhygienic social conditions as causative factors. The infectious diseases mentioned may be active either through devitalizing and debilitating the germinative organs and germ cells of the parents, or the children themselves may be affected.

In both of my above reported cases severe rheumatic polyarthritis was present in the mothers during gestation; therefore I am inclined to consider this infection as a factor that had some bearing upon the anomaly in the newborn.

Children who have long suffered from severe tuberculosis in any part show often signs of retarded development, and spinal caries is a comparatively common cause of this retardation (Marie and Leri, "infantilisme pottique").

According to Hertogh's views, the thyroid would hold a central etiologic position even in the presence of these causes, inasmuch as only a preëxisting disturbance of the thyroid function or one provoked by these agencies (lues, tuberculosis, etc.) could bring into existence an infantilistic stunting of growth. However, this exclusive standpoint can no longer be maintained in the face of clinical evidence. As Ferranni has pointed out, many cogent reasons argue against Hertogh's extreme standpoint.

The dependency of dystrophic infantilism upon malarial infection is evident from its comparative frequency in malarial districts.

Ferrannini, in Sicily, and H. de Brun, point to the numerous emaciated dystrophic individuals of small figures and senile countenances among those who have suffered from malaria in early life. I made similar observations in Syria.

Differing from the pure type of Lorain, these persons have an enormous abdomen, due to the intumescence of spleen and liver. Grotesque figures result from this contrast of general emaciation and enormous abdomens.

Orgeas shows us the stunting effect of parental malaria upon the offspring of Europeans in French Guiana. He emphasizes the extreme smallness of the body, the flabby skin, the atrophy of the male genitals, and microcephaly as main features of these "variations morbides." This degeneracy of the children, especially the males, due to chronic malaria and deterioration of the parents, is one of the chief causes of the extinction of the unmixed white race in the tropical (malarial) lands.

Another factor, causative of dystrophic infantilism, is chronic disturbance of the gastro-intestinal tract, with consequent malnutrition and cachexia.

However, we must not lose sight of the fact that infantilism itself from any cause may predispose to intestinal insufficiency or to other diseases, as tuberculosis, forming thus a vicious circle.

Babies with poor digestion and assimilation remain puny and meager for long time, and their mental growth is retarded also. Fortunately this delay in most cases is only temporary. But in more severe cases the affected individuals remain small, puny, dystrophic in the full sense of the term. One also observes this occasionally among those prematurely born, especially if nourished insufficiently and artificially.

Herter, in a monograph (1908), describes several children, all underdeveloped, due to intestinal disturbances with a characteristic intestinal flora, (*Bacillus bifidus* Tissier and *Bacillus infantilis*), and similar cases are reported by Freeman, Heubner, and Schulz.

M. Landolfi reports an interesting case of infantilism of gastric origin. The patient, aged twenty years, was the size of a ten-year-old boy; the stunted growth was due to gastrosuccorhea of long standing.

In addition to the etiologic factors mentioned so far, affections of various other parenchymatous organs have been accused as the cause of infantilistic forms (*vide* table of Anton).

Byron Bramwell describes a case as infantilismus pancreaticus. Male, eighteen and one-half years old, with the aspect of an eleven-year-old boy. The epiphyseal cartilages still unossified. The cause of this inhibition of growth was a chronic diarrhea for nine years. Under treatment with pancreas for two years, the boy grew $5\frac{7}{8}$ inches and gained $23\frac{3}{4}$ pounds; the sexual development became normal.

A similar successfully treated case is recorded by J. L. Renroul.

Morlat reports an observation of infantilism produced by insufficiency of the suprarenals, with great improvement by administration of suprarenal extract. Thyroidin was ineffective.

The dependency of the sexual function upon the suprarenals is well known from its disturbance in Addison's disease. Tandler found in cases of Addison's disease alterations of the interstitial cells and in the germinative part of the testicles, and similar changes in the testicles of a man with primary hypoplasia of the suprarenals. Wiesel and Karakaschew and others describe retardation of the sexual characters in hypoplasia and atrophy of the adrenals. The case of Recklinghausen is even more convincing, since in the above cases one might consider the hypoplasia of the adrenals and genitals as coördinate symptoms, due to a common cause. Recklinghausen's case concerned an eighteen-year-old dwarf, 95 cm. in height, $10\frac{1}{2}$ kilos in weight, with the appearance of a four-year-old boy. The postmortem revealed caseous inflammation of both adrenals. Recklinghausen considers the possibility of a connection between dwarfism and degeneration of the suprarenals.

It might not be amiss here to point to the connection between premature sexual development in children as early as from one to seven years of age, and the adrenals. From the literature one may gather that a sudden and rapid genital and general physical development with secondary sexual characters in young children was encountered especially in those cases, that showed at autopsy tumors of the adrenals and kidneys (hypernephroma) (Bullock and Sequeira).

Finlayson gives a report of a twenty-three-year-old man, who suffering from biliary liver cirrhosis, had a weight of only 35½ kilos. His brother, aged nineteen years, likewise suffering from biliary liver cirrhosis, had a weight of 31 kilos.

Hasenclever published three cases of infantilism suffering from liver cirrhosis. Additional cases are reported by Gilbert and Fournie, Lereboullet, Cautley, and others.

Otto May speaks of renal infantilism in congenital or early acquired affections of the kidneys, chronic interstitial nephritis and diabetes insipidus. (Miller and Parson, Fletcher, A. Naish, Miller, Sutherland.)

Weber and Cherry contribute observations pertaining to this category of infantilism.

Finally, also primary disturbances of the brain, as encephalitis, porencephaly, microcephaly, paralysis progressiva in early life exert an inhibitory, detrimental influence upon the development of the whole body.

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STUDIES ON THE SMEGMA BACILLUS

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PART I.—LITERATURE.

INTRODUCTION. Closely following the discovery of the tubercle bacillus by Koch, in 1882, other workers announced the finding of bacilli resembling the tubercle bacillus in staining and morphological characteristics. Several claim credit for this discovery—all working and reporting at about the same time—chief among whom are Alvarez, Czapslewski, Doutrelepon, Laser, Matterstock, and Tavel. Only one year earlier, in 1884, Koch had suggested the idea and possibility of there being several other bacilli with staining properties similar to those of the tubercle bacillus.

SMEGMA BACILLUS. This newly discovered bacillus—the smegma bacillus or *Bacillus smegmatis*—came in apparent answer to this prophecy, and was doubly confusing because it resembled the tubercle bacillus not only in its chief and heretofore distinctive characteristic—its staining properties—but also in its morphology. This confusion and difficulty were likely to be encountered in bacteriological examinations of urine where mistaken diagnoses have probably resulted in many useless but serious operations.

We are indebted to Dr. M. P. Ravenel, director of the laboratory, for assistance and advice during the progress of this work and in the preparation of this paper.

The work divides itself into two main parts: (1) a study of the available literature, which is scarce as well as conflicting, and (2) the laboratory work.

OCCURRENCE. The smegma bacillus is found widely distributed over the surface of the human body. It appears in especially large numbers in any place where the normal skin secretions are allowed to collect, as about the genitalia, under the foreskin in males, and between the labia in the female, about the anus and the perineum of both, in the umbilicus, in the cerumen of the ear, about the teeth, etc. In this respect its occurrence is dependent upon the degree of cleanliness of the patient. It also appears in the urine—more abundantly in females—where, according to some writers, it may be found in 59 per cent. of the cases, while others report it as rarely present, especially in urine from males. It has also been

reported present in sputum and lung cavities in cases of gangrene of the lungs and fetid bronchitis. One case has been reported of an ovarian cyst in which bacilli very similar to if not identical with the smegma bacillus were found, which were thought to have been there by perforation from the rectum or by digital examination.

The occurrence about the genitalia and possibility of gaining entrance into the urine, where they might be mistaken for tubercle bacilli, resulting in a diagnosis of genito-urinary tuberculosis, forms the chief point of practical consideration in the study of the smegma bacillus. This source of contamination of urine, however, is not deep-seated, since no writer reports finding smegma bacilli in the bladder or the deeper portions of the urethra. On the other hand, several report unsuccessful attempts to find them there.

One investigator reports work done on animals in which he found the smegma bacillus about the genitalia of horses, dogs, cattle, guinea-pigs, and white rats. The cat and rabbit gave negative results. In smear preparations, several note the tendency of the bacilli to be found more abundantly in and about epithelial cells or other debris.

MORPHOLOGY. The difficulty and uncertainty of cultivation necessitate greater dependence on microscopic findings, but it is here that we find the close resemblance of the smegma bacillus to the tubercle bacillus, and morphology presents one of the two chief possibilities of confusion.

It varies widely in morphology, but usually is 3 to 5 μ long by $\frac{1}{4}$ to $\frac{3}{4}$ μ wide: a rather long, slender, often slightly curved bacillus or little rod with rounded ends. Its morphological variations seem no more limited to one dimension or property than to another. It may be about the same length as the tubercle bacillus as ordinarily found in human sputum—much shorter, much longer—or we may find some preparations with only straight bacilli, or others almost entirely composed of small curved rods, some thicker, some thinner. The short bacilli often appear like comma bacilli. Some authors claim the form and size are dependent on the kind of culture media used. One author suggests that the degree of curvature is apparently dependent on the position of the bacillus in the colony—those nearest the centre being most curved, while those farther out and composing filaments are straight. A wider variation from cultures is only to be expected from, and certainly would tend to strengthen the doubt in, the fact that the organism has not yet been cultivated, at least not so frequently and generally as claimed.

Dahms claims never to have found a "smegma bacillus showing in a typical way the peculiar sharp curve near one extremity which is so frequently observed in tubercle bacilli."

Many claim to have found so-called "spores," "spore bodies," "sporogenic bodies," etc., appearing at each end of the stained bacillus, taking a deeper stain and giving to short bacilli at least

the appearance of diplococci or of two cocci lying close to each other. Preparations from colonies on media producing rapid growth show evidence of manner of growth and development. Scattered among the bacilli throughout the field are to be found numerous short, oval segments or egg-shaped bodies of the same color as the bacilli, but quite separate and distinct from them. Also other bodies—little rods intermediate in size between the egg-shaped segments and the mature bacilli—are found and seem to be an intermediate stage of development. Some report finding granular bacilli on certain kinds of media, especially Löffler's blood serum, while others claim never to have seen granular forms. Hang-drop preparations show absence of independent motion.

STAINING. Staining is the second important point in which the smegma bacillus resembles the tubercle bacillus, and this is second in order of enumeration only, because in order of importance it really holds first place. Like the tubercle bacillus, the smegma bacillus belongs to the class of so-called "acid-fast," *i. e.*, it resists decolorization by acids after staining with carbol-fuchsin. Herein lies the real difficulty for the clinician, for the test long held for the tubercle bacillus was this property of acid-fastness. Then the discovery of the smegma bacillus introduced a source of error in that in certain cases, as for instance in the examination of urine for tubercle bacilli, the mere finding of red bacilli after decolorization, was not sufficient basis for diagnosis of genito-urinary tuberculosis, because it might be the smegma bacillus. Immediately several workers undertook the problem of devising a method whereby an accurate differential diagnosis could be made between these two similar organisms, and their attempts, especially those of the earlier workers, were to stain it under two conditions: in tissue and in smear preparations.

These efforts proved successful in quantity but of doubtful success in value, since scarcely any two workers have reached the same conclusions. Yet each has proposed and enthusiastically advocated some method quite different from all others, and one which he is sure will prove reliable in all cases at all times. As a rule, he has been equally enthusiastic and urgent in his disapproval of all other methods of differentiation by staining or otherwise. At the present time no absolutely reliable method of differentiation by staining properties has been found, and yet more than twenty different methods have been advocated by the originator of each. The cause of this wide variation in results is found primarily in the variable staining properties of the smegma bacillus, and possibly secondarily in the fact that no one observer has done sufficiently extensive work to prove the inaccuracies of his own method. More recent writers suggest the impossibility of a differential method of staining due to the variation in the staining reactions of the smegma bacillus and its close relationship to the tubercle bacillus.

The numerous methods thus far suggested have, in the main, agreed upon and been based on two points: (1) that the smegma bacillus stains with difficulty but is equally slow and difficult of decolorization, and (2) that it possesses both these properties to a less extent than the tubercle bacillus. Several observers have mentioned variation in staining reaction dependent on the nature of culture media or stage of subculturing. For instance, some claim the acid resistance to be greater when the organism is grown on drier culture media, and others claim each successive transfer or subculture shows a gradually decreasing degree of acid-fastness. A. Moeller, though, claims the smegma bacillus to be absolutely acid-alcohol-fast, not decolorized by twelve minutes' application of 3 per cent. HCl-alcohol and not diminished in this property after twenty-five generations.

Possibly the best idea of the various methods is obtainable from a summary and classification used by Drs. Young and Churchman. A brief form of their classification follows:

I. *Methods Depending on Greater Avidity of Smegma Bacillus for the Stain.*

(a) Method of Giacomi: Specimen in carbol-fuchsin heated barely to steaming; smegma bacilli deeply stained; Tubercle bacilli not at all or only faintly stained and easily decolorized.

II. *Methods Depending on Decolorization without Alcohol.*

(a) Method of Gabbett: Specimen heated in carbol-fuchsin, washed in water, decolorized, and counterstained with Gabbett's solution of methylene-blue, H_2SO_4 , and water.

(b) Method of Ziehl-Neelsen: Specimen heated in carbol-fuchsin, washed in water, decolorized by H_2SO_4 , and counterstained in aqueous methylene-blue.

(c) Method of Fränkel: HNO_3 replacing H_2SO_4 in (a).

(d) Anonymous method (recommended by Alvarez and Tavel): Glacial acetic acid replacing H_2SO_4 in (a).

(e) Method of Kühne: Carbol-fuchsin to stain, HNO_3 to decolorize, and picric acid to counterstain.

(f) Method of Weigert (modification of Gram's method): Stained and treated with KI solution as in Gram's method. Anilin oil to decolorize.

(g) Method of Giacomi: Heated in distilled water containing two to three drops of concentrated alcoholic fuchsin, wash in weak solution of perchloride of iron and then decolorize in concentrated solution of the same.

III. *Methods Depending on Decolorization with Alcohol Alone.*

(a) Method of Gram: Stain with aqueous solution of gentian violet, then with Gram's solution of KI, decolorize with absolute alcohol.

(b) Method of Weichselbaum: Stain in carbol-fuchsin, decolorize, and counterstain with concentrated methylene-blue in absolute alcohol.

(c) Method of Czaplewski: Carbol-fuchsin to stain, wash for five minutes in fluorescein methylene-blue, then for one-half to one minute in concentrated methylene-blue.

(d) Method of Pappenheim: Stain in carbol-fuchsin, then dip three to five times in solution consisting of absolute alcohol, corallin methylene-blue, and glycerin. Tubercle bacilli are stained red and smegma bacilli blue.

IV. *Methods Depending on Decolorization with Alcohol and Another Agent.*

(a) Method of Koch and Ehrlich: Stain for twenty-four hours in anilin water fuchsin (or gentian violet). Transfer to HNO_3 , one to four. Place in 60 per cent. alcohol for a few seconds, wash, and counterstain with methylene-blue (or vesuvin).

(b) Method of B. Fränkel: Stain with carbol-fuchsin, decolorize with a mixture of HNO_3 , alcohol, and methylene-blue.

(c) Method of Marzinowski: Stain in watery solution of carbol-fuchsin. Counterstain and decolorize with Löffler's methylene-blue.

(d) Method of Lustgarten: Stain twelve to twenty-four hours in concentrated alcoholic solution of gentian violet mixed with aqueous solution of anilin oil. Wash in absolute alcohol, ten seconds in 1.5 per cent. solution of potassium permanganate, then in concentrated aqueous solution of pure sulphurous acid (freshly made by action of H_2SO_4 on metallic copper). After disappearance of precipitate of manganese oxide, repeat permanganate, sulphurous acid, and water until decolorization is complete.

(e) Method of Alvarez and Tavel: Same as (d) except oxalic acid instead of sulphurous. Also counterstain with saponin, eosin, or picrocarmin.

(f) Method of Honsell: Carbol-fuchsin stain, wash, place in acid alcohol (3 per cent. HCl in absolute alcohol) ten minutes, wash, counterstain with alcoholic methylene-blue.

(g) Vesuvin and malachite green have also been advised (by Fränkel) and magenta and chyrsoidin (by Gibbs).

V. *Methods Depending on Preliminary Treatment Aimed at Diminishing Resistance to Decolorization.*

(a) Method of Matterstock, Bitter, and Markuse: Preliminary solution of fatty substances by ether or chloroform. Stain as usual.

(b) Method of Gottstein: Heat specimen with KI in alcohol, wash in alcohol and water; the fatty substances are removed and the specimen is then stained as usual.

(c) Method of Bunge and Trautenroth (method for spores): Fix specimen and remove fat by absolute alcohol. Then treat with 5 per cent. chromic acid, stain with carbol-fuchsin, decolorize with dilute H_2SO_4 then with pure HNO_3 , counterstain with concentrated alcoholic methylene-blue.

CULTIVATION. Cultivation of the smegma bacillus is one of the most fruitful sources of confusion and difference of opinion among

various workers. Laser, in 1897, claimed to have cultivated it and Czaplewski, a little later, claimed to have secured the first pure cultures. Others followed quickly with similar claims, but more recent workers and the growing consensus of opinion seems to discredit these claims, believing that some other members of the acid-fast group instead of the smegma bacillus were cultivated.

The finding of these men and others who have claimed its cultivation was the result of accident, their purpose usually being to cultivate gonococci or to find a cause of syphilis.

The uncertainty about the reliability of their results is strongly substantiated by both the widely differing results and the ease with which some have obtained growth on almost any kind of culture media, as contrasted with the absolute inability of others to get any growth whatever. A brief summary of their claims, is here given:

The first cultures were made upon agar plates and slants which had been smeared with sterile human blood and incubated twenty-four hours to prove sterility before inoculation. Growth resulted in small colonies like diphtheria or streptococcus. Transplanted to blood-serum and glycerin-agar the growth continued in the same small almost dew drop-like colonies. Most investigators report a difference in cultivation between smegma bacilli and tubercle bacilli in that the smegma bacillus grows more rapidly—a few reporting several days required—but it is usually reported as growing within twenty-four hours to a few days.

The growth on different kinds of media is as follows:

Agar smeared with sterile human blood: numerous, small, diphtheria or streptococcus-like colonies showing mainly micrococci, but after several days are found a few, small, irregularly rounded, grayish-white colonies which prove to contain smegma bacilli.

Gelatin: No development. Some claim slight growth of rather short bacilli, often curved and knotted or with ends swollen in club-like swellings. Weber claims the growth to be composed of quite large bacilli.

Agar slants and plates: Sparse growth after several days at 37° C.

Peptone water and bouillon: Scarcely noticeable growth of a flocculent grayish color.

Glucose bouillon: Marked development in twenty-four hours. White sediment loosened in shreds on shaking. Moeller claims a dry pellicle-like growth floating on the surface of the bouillon, which sinks to the bottom in fragments on shaking.

Potatoes: No visible growth after three days, but rather long bacilli found on scraping the surface for a smear. Later scanty growth, yellowish layer, irregular shape, and indefinite outlines. Weber characterizes the bacillus grown on potato as short and almost coccus-like. He also claims better growth if the potato is alkaline in reaction.

Nutrose-serum agar (used for Czaplewski's first culture): Numerous, small, irregularly rounded colonies of rather long bacilli.

Glycerin agar: Twenty-four hours showed distinctly visible growth, a grayish, well-defined layer. Forty-eight hours showed thick, grayish-white, or yellow growth, margins sharply defined, indented and lobulated appearance, centre darker.

Löffler's serum: Twenty-four hours gave scarcely visible growth. Forty-eight hours, a yellowish-gray color. Variable size from mere specks to areas 2 mm. in diameter, which by confluence later formed a distinct layer. Bacilli often appear granular and as short rods.

Glycerin-milk agar (used and prepared by Neufeld): Claimed to reproduce more nearly the natural conditions of nourishment and to resemble smegma so closely that the bacilli grown on it are more like those observed in direct smear preparations, *i. e.*, some claim that a shorter, plumper bacillus grows on this medium.

Milk medium seems especially likely to produce a growth characterized by an abundance of pleomorphic forms. It is not coagulated, however, by the growth.

Weber reports the successful use of lanolin agar, claiming growth in sixteen out of eighteen cases showing smegma bacilli in one series examined. Stab cultures in agar and gelatin show limited extent of growth which is quite closely confined to the path of the needle. All agree upon an optimum temperature of 37° C.; no growth below 23° C.

The microscopic appearance of a colony of smegma bacilli (especially with the large flat colonies found on glycerin-agar) is wax-like, white or nearly so, dense, finely granular, and with sharply defined margins. The colonies are not always circular, yet never sharply angular, but their irregularities consist of rounded and lobulated extensions. The higher power of the microscope used on a stained impression smear from one of these colonies shows very well the arrangement of the smegma bacilli in the colony, often quite like tubercle bacilli. The bacilli may be in straight lines end to end, as portions of concentric circles, or branching from each other at various angles or forming long parallel lines.

PATHOGENICITY. On one point every investigator presents the same report, and that is the pathogenicity of the smegma bacillus. All agree in saying that it is a harmless, non-pathogenic organism, *i. e.*, a saprophyte. All pieces of work are practically a unit on this, that animal inoculation fails entirely to produce any serious results. Some claim, though, that a slight tubercle-like swelling or nodule is produced at the point of inoculation.

The one case reported by Dietrich of finding smegma bacilli in an ovarian cyst would seem to indicate the possibility at least of the organism possessing some pathogenicity. As mentioned above, the probable explanation of this case is the entrance of the bacilli by digital examination.

It might be added that the unity of opinion on the question of pathogenicity does not seem to verify the claims of cultural findings; for if others than the true smegma bacillus were really cultivated, they were all of the same class, harmless acid-fast, and hence unable to give positive inoculation results.

PART II.—LABORATORY WORK.

The laboratory side of this paper, undertaken with a view of determining the prevalence of the smegma bacillus about the male genitalia and of verifying some of its cultural and staining properties, must from the nature of the object as thus stated divide itself into two main parts: The first consisted of collecting smegma from which smears were made to be stained and tabulating results of urinary examinations in this laboratory during the past two years. The second consisted in taking swabs or collecting larger amounts of smegma to be used for planting out on several kinds of culture media in an attempt to grow the smegma bacillus.

For this material, access was kindly granted to the male wards of the Wisconsin State Hospital for the Insane and the Dane County Asylum, and to Drs. Lorenz and Stebbins for kindness and coöperation, thanks are gladly extended.

Tabular form¹ will best show the results of each piece of work, preceded by a brief explanation of method or technique used, and followed by summary of results obtained. The first series will consist of a number of cases from which smear preparations were taken, stained, and studied. No complicated plan or procedure was required for this. The inmates were simply taken one at a time, the penis examined for presence of smegma in sufficient quantities for the purpose of this study, and then a number of smears were made on glass slides, banded together and numbered. Or if, as was true in many cases, the smegma found was the product of too long accumulation and therefore too thick and dry to be smeared out at once, a sufficiently large piece was removed and taken to the laboratory to be mixed with sufficient sterile water to make the required number of smear preparations. Then these, together with the rest, were fixed by heat and stained as follows: one in a borax solution of methylene-blue; one in carbol-fuchsin followed by decolorization with 25 per cent. H_2SO_4 until the slide presented the same appearance of decolorization as is usually presented by a slide of sputum stained and decolorized for tubercle bacilli, and then, after examination, counterstained in borax methylene blue (the oil being carefully removed with xylol before counterstaining); one in carbol-fuchsin followed by decolorization with acid alcohol

¹ Detailed tables omitted on account of length.

(5 per cent. HNO_3 , 70 per cent. of 95 per cent. alcohol, 25 per cent. H_2O) until the slide presented usual pale appearance; and one in carbol-fuchsin, followed by decolorization with Labarraque's solution until the slide had assumed a distinct brown color.

All carbol-fuchsin staining was done with Ziehl's carbol-fuchsin for twelve hours in a paraffin oven at 50°C . or twenty-four to thirty-six hours at room temperature.

No. of cases.	Stain.	Decolorizer.	Counterstain.	No. showing smegma bacilli.	No. not showing smegma bacilli.
126	Carbol-fuchsin	H_2SO_4	None	85	41
112	Carbol-fuchsin	H_2SO_4	Methylene-blue	19	107
196	Carbol-fuchsin	Acid alcohol	None	16	103
117	Carbol-fuchsin	Labarraque's solution	None	16	101

SUMMARY OF TABLE. Of 127 cases taken, practically all present the same picture when stained with methylene-blue. A number of different kinds of cocci and bacilli are present in abundance, the predominating organism always being mentioned first. Many of the bacilli are diphtheroid in appearance. The chief difference between any one slide and another is simply a matter of degree and proportion of each kind of organism, each having the same types.

Of 126 stained with carbol-fuchsin and decolorized with 25 per cent. H_2SO_4 , 41 cases, or 32.5 per cent., failed to show any red bacilli at all, while 85 cases, or 67.5 per cent. showed red bacilli in greater or less abundance as described under each case as to size, shape, etc.

Of the same 126 cases counterstained with methylene-blue, 85 of which had shown red bacilli before counterstaining, only 19 cases, or 22 per cent., continued to show them in greater or less numbers, *i. e.*, 77 per cent. of the cases showing red bacilli before counterstaining lost or had their red stain masked when counterstained.

Of 119 cases stained with carbol-fuchsin and decolorized with acid alcohol, 16 cases, or 13 per cent., showed a few or more red bacilli, usually very faint red or in larger masses of debris in the preparation which had not been so thoroughly subjected to the action of the decolorizer.

Of 117 cases stained with carbol-fuchsin and decolorized with Labarraque's solution, 16 cases, or 13 per cent., showed red bacilli in varying numbers and in varying stages of decolorization from faint red almost decolorized to dark red bacilli, as yet unmodified by the action of the decolorizer.

Since the material in the above series was secured from a class of men whose condition would mean habits of cleanliness not up to the average standard, a series of 20 cases from normal men was studied, somewhat as a control for results of the first series. The

subjects from whom these specimens were obtained were men about the laboratory, faculty, and students.

Material was collected as for the first series, save that only H_2SO_4 was used as a decolorizer, the purpose being merely to determine the presence or absence of smegma bacilli.

Of 20 cases studied in this second series, 13, or 65 per cent., showed the presence of smegma bacilli when stained with carbol-fuchsin and decolorized by 25 per cent. H_2SO_4 . This is to be compared with 67.5 per cent. in the first series.

Two cases, or 10 per cent. of all cases, still continued to show smegma bacilli even after counterstaining. This corresponds to 14 per cent. similarly obtained in the first series.

Methylene-blue used alone showed the same results as in the first series.

URINE. From an interest in the findings and conclusions of Young and Churchman that urine could not be safely collected unless by their method, which provides for previous urethral irrigation, and the conflicting statement of other writers that catheterization is sufficient, a study of the case records of this the State Laboratory of Hygiene has been made. This covers a period of the past two years, and includes all the cases of urine examined for tubercle bacilli, whether this examination was especially requested and indicated by history and suspicions of genito-urinary tuberculosis or was simply made as a part of the routine examination of urine.

The results of this study are tabulated below:

Findings.	To be examined for tubercle bacilli.	Routine examination.
Positive to tubercle bacilli	3	2
Negative to tubercle bacilli	10	18

This shows 22.5 per cent. of cases of suspected tuberculosis to show acid-fasts and 10 per cent. of cases not suspected, or 14 per cent. of all cases examined for tubercle bacilli. These cases are taken as they came into the laboratory from all over the State, without special precaution or technique to avoid getting smegma bacilli into the urine, and probably few were collected by catheter.

Young and Churchman report 11 cases out of 24 collected similarly as positive, or 45 per cent., as compared with 14 per cent. found here, including more than one-third of the cases in which diagnoses of genito-urinary tuberculosis had already been made or suspected. This would tend to show less chance of the smegma bacilli getting into the urine than these workers suggest.

CULTIVATION. *Technique.* The second portion of the laboratory side of this study consists of a series of cultures from 42 cases, taken in different ways, treated differently, planted differently, and incubated differently in an effort to produce growth.

The material for the first 32 of these was collected from the penis by the usual sterile swab used for the taking of cultures and planted on various kinds of artificial culture media—meat-lactose-agar, human hemoglobin-agar, cat-blood agar, blood-serum, meat plain agar, and meat-glucose-agar. Cultures were incubated at 37° C. aëroically or anaëroically, as the case might be, until examined. Examination of smear preparations was made after varying periods of two days to two weeks, and with two staining methods. One preparation was stained with borax methylene-blue and the other with carbol-fuchsin, followed by 25 per cent. H_2SO_4 to decolorize, then examined, counter-stained with methylene-blue, and again examined.

The technique for the last ten cultures differed slightly from the first series. The antiformin method for isolation of tubercle bacilli was used on large quantities of smegma taken from several of the more abundant cases and the sediment planted out on Dorset's egg medium, three or four loopfuls each to the first two tubes and the remainder poured into the third.

RESULTS. Of the 42 cases studied, the first 32, or those planted as from ordinary swabbing, show but little difference save the 6 grown anaëroically, and these seemed to have slightly less abundant growths. In all cases, however, the growth was quite abundant, and upon examination proved to contain the same organisms, cocci and bacilli, of several kinds and in varying proportions. Very often bacilli were found which were so like diphtheria bacilli that a differentiation could be made only with difficulty, if at all. Many others, while not resembling the diphtheria bacillus so closely as to be called pseudodiphtheria, still were enough like to to be called diphtheroid. These are probably the same organisms mentioned by several observers in their writings on the smegma bacillus.

Stained for acid-fasts, these same preparations failed to show any organisms which had resisted decolorization, only a few doubtful ones being found, and these were quickly proved negative on counterstaining.

The last 10 cases treated by a method calculated to eliminate the abundant growth of other bacilli and cocci failed to show any better results, save that the growth was less abundant.

CONCLUSIONS. From the foregoing we can see several conclusions quite clearly set forth for us, not least among which is the need for a thorough, comprehensive, dependable piece of work on this subject.

From the knowledge at hand it is evident that:

1. The smegma bacillus resembles the tubercle bacillus very closely in staining properties and in morphology.
2. No method of differentiation by staining is entirely adequate for all cases.
3. The successful cultivation of the true smegma bacillus is open to question.

4. Successful cultivation granted, the inherent difficulties by methods now available render this method of differentiation of little value in routine diagnosis.

5. The smegma bacillus is found in a large proportion of patients examined, but the widespread occurrence is quite dependent on the degree of cleanliness of the patient, together with the presence or length of foreskin in males.

6. By thorough cleaning of the genitalia, especially the meatus and by catheterization, urine to be examined for tubercle bacilli can be collected with a fair degree of certainty of freedom from smegma bacilli.

7. With the above precautions, the finding of acid-fast organisms after decolorization with acid-alcohol enables us to make a presumptive diagnosis of genito-urinary tuberculosis.

8. Final differentiation, however, can be made only by animal inoculation.

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REVIEWS

INFECTIONS OF THE HAND. A GUIDE TO THE SURGICAL TREATMENT OF ACUTE AND CHRONIC SUPPURATIVE PROCESSES IN THE FINGERS, HAND AND FOREARM. By ALLEN B. KANAVEL, M.D., Assistant Professor of Surgery, Northwestern University Medical School, Chicago. Second edition; 463 pages; 147 illustrations. Philadelphia and New York: Lea & Febiger, 1914.

AFTER disposing of simple localized infections, as paronychia, carbuncle, etc., in Part I, the remainder of the book discusses the grave infections as tenosynovitis, fascial-space abscesses, lymphangitis, and their sequelæ from the anatomical and clinical stand-points. The tendon sheaths of the fingers with their communications and the extensions into the radial and ulnar bursæ are described. Five well-defined fascial spaces are exposed: the middle palmar, the thenar, the hypothenar, the dorsal subcutaneous, and the dorsal subaponeurotic. The relation between the tendon sheaths and the palmar spaces is considered. About this outline revolves the theme of the whole book.

The faults of the work are insignificant as compared to its merits. Of the former the chief ones are repetition and lack of a careful finish from the stand-point of uniformity of nomenclature and expert proof-reading. Chapter XV, which gives excerpts from the literature, might well be omitted. It consists of literal translations from French and German authors. It is difficult to understand why English and American authors are entirely neglected. By better arrangement of its contents and avoidance of repetition, as for example the description of the treatment of infections once instead of several times, the bulk of the book could be advantageously reduced. Several omissions and statements occur to which we believe exception may be taken. For example, a noteworthy omission is the differential diagnosis between traumatic neuritis from direct trauma to the nerve (usually the median) in a punctured wound and actual infection of the hand. The author "condemns most severely" the excision of a carbuncle. In cases of grave septicemia from this cause it appears to be just as rational *immediately* to prevent further absorption of toxins by excision of a carbuncle with cauterization of its base as it is

to amputate a putrid limb under similar conditions. We are not aware that streptococci produce pus, but we do know that they are frequently forerunners of the pyogenic staphylococci. While we agree that isolated necrosis of a metacarpal is commonly tuberculous, we disagree as to its frequency in syphilis, since in our experience the latter disease produces a characteristic *proliferative osteoperiostitis*. The sentence: “. . . temperature running a classical hectic curve (98° to 102° F.), then constantly between 120° and 130°, having the appearance of impending death” possesses a little ghastly humor. Blood-counts are not usually estimated in centimeters but in millimeters.

The masters Tillaux, Malgaigne, and Cannon are named Tilleau, Tilleaux, Malgaine, and Canon respectively. The references to some of the figures are wrong and sometimes leaders and legends are missing. It would facilitate references to mention the pages on which the figures appear.

The value of the monograph cannot be overestimated. After carefully reading it there is no excuse for the operator who does not immediately get better results with his cases of infected hands. So far as the wage-earner is concerned a restoration to complete function in 95 per cent. of the abscesses of the fascial spaces and the reduction of the morbidity in tendon-sheath infections by one-half are matters of superlative economic importance. It may readily be seen that the message the book carries must eventually promote the weal and welfare of humanity. P. G. S., JR.

CLINICAL DIAGNOSIS. BY CHARLES E. SIMON, B.S., M.D., Professor of Clinical Pathology and Experimental Medicine, College of Physicians and Surgeons, Baltimore. Pp. 809; 210 illustrations. Eighth edition. Philadelphia and New York: Lea and Febiger, 1914.

It is fortunate indeed that such an early demand for a new edition of Simon's *Diagnosis* should have arisen. It has given the author an opportunity to introduce a wealth of new material, the product of the last two years, as well as to carefully revise the old.

The quantity and quality of the new material is of special interest and brings one up to the minute in laboratory diagnostic technique. It includes a concise and lucid account of the diagnostic methods dependent on the appearance of the protective ferments of Abderhalden in the blood and opens the gates to this new and attractive field of "organ diagnosis."

The Wassermann reaction has received a thorough rewriting,

with special emphasis on the desirability of uniformity in the various reagents, notably the antigen. The compliment-fixation test in latent gonococcus infections has been included in this edition.

In the discussion of the functional tests of the kidney the author declares himself for the phenolsulphonephthalein test and wisely confines himself to a description of this test alone. He shows that its use is practicable and urges its adoption by the general practitioner.

The division of the book into two sections, the first dealing mainly with technique and the second with the application of this information in concrete diseases, is continued in this edition. This description of the correct interpretation of laboratory data, under varying clinical conditions, is invaluable and will appeal especially to those who are depending on others for their laboratory work.

The present arrangement of the book, the character as well as the happy presentation of the information it contains, assures its continuance in the forefront of works of its kind. A. A. H.

MEDICAL GYNECOLOGY. By S. WYLLIS BANDLER, M.D., Adjunct Professor of Diseases of Women, New York Post-Graduate Medical School and Hospital. Third edition; pp. 790; 150 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

THE practical value of a book of this nature is attested by the appearance of a third edition. A thorough revision has included the more important advances of the five years which have elapsed since the second edition was published. The most extensive revision occurs in the chapter on internal secretions, where the author details our present knowledge of the relationship between the glands of internal secretion and the genital tract of women, and refers to the merits of organotherapy. The broader aspects of certain cases are set forth in a notable chapter on the associated nervous conditions in gynecology. Mention must also be made, especially as regards the sections on treatment, of the chapters dealing with constipation, the anomalies of menstruation, and gonorrheal infections. The author considers it as essential that the public be educated concerning the early symptoms of carcinoma.

As a very complete and effective presentation of practical non-operative measures in gynecology the book will be of much service to all engaged in this branch of medicine. P. F. W.

THERAPEUSIS OF INTERNAL DISEASES. Edited by FREDERICK FORCHHEIMER, M.D., Sc.D. (Harv.), Professor of Medicine, Medical Department, University of Cincinnati (Ohio-Miami Medical College). Four volumes and a desk index. Vol. I, pp. 795; 67 illustrations. Vol. II, pp. 874; 35 illustrations. Vol. III, pp. 984; 41 illustrations. Vol. IV, pp. 942; 45 illustrations. New York and London: D. Appleton and Company, 1913.

DURING the past five years several admirable systems of therapeutics have been published in this country. The last and most comprehensive of these works to appear is *Therapeusis of Internal Diseases*, edited by Frederick Forchheimer. Although this work embraces four volumes, none of the volumes contains more than a little over nine hundred pages, and their size prevents them from being in any sense cumbersome. The addition of a desk index in a small separate volume adds materially to the convenience and ease with which the books can be used.

As must be the case in so extensive a work, the various subjects, which include practically the whole realm of internal medicine, are discussed by a large number of different authorities. Here the word "authorities" may with propriety be used in its literal sense, for a survey of the list of collaborators discloses the fact that in nearly every instance those selected to contribute to these volumes have been eminently qualified for the tasks assigned them. In spite of the diversity of subjects discussed by such a number of different authors a surprising degree of uniformity has been obtained, a fact which implies that the entire work has been subjected to exceedingly careful editorial supervision. Indeed, throughout all the volumes, especially when differences of opinion exist, pertinent editorial notes and comments abound.

The first volume is devoted to the fundamental principles of general therapy, and consists of a group of noteworthy contributions which furnish a firm and sound foundation for the special therapeutic considerations which are contained in the other volumes. All the chapters in this volume are of importance and interest, but among those which are conspicuous may be mentioned that on organotherapeutics by Reid Hunt, Francis Carter Wood's admirable discussion of vaccines and serum therapy, climatology by Henry Sewall, and the contributions of Warren Coleman on nutrition and dietetics, and of Victor C. Vaughan on toxicology. Hydrotherapy, exercise, and various forms of mechanotherapy, as well as radium and the x -rays and psychotherapy, are all given careful consideration.

In the remaining three volumes special therapy is taken up. This comprises a detailed discussion of the treatment of all the diseases included under internal medicine. Volume II deals with

the treatment of the acute infections, the intoxications, and constitutional diseases. One of the most complete contributions under the infections is Frederick C. Shattuck's discussion of typhoid fever, in which he advocates a liberal dietary, although he belittles the necessity of basing such a diet upon definite caloric values. Henry L. Elsner has written an excellent article on the treatment of pneumonia, in which he takes a decided stand in favor of the open-air treatment of this disease. Gottheil's article on syphilis is also worthy of note, as are the contributions of John Ruhräh on smallpox and vaccination. Under the intoxications are discussed alcoholism, opium, phosphorus, food poisoning, pellagra, and intestinal auto-intoxication. The section on constitutional diseases is wholly excellent, as might be expected when the contributors of these chapters are considered. Charles Lyman Greene writes on the difficult subjects of myositis, gout, and arthritis deformans. Davis Riesman's consideration of diabetes mellitus and diabetes insipidus is admirable, and obesity and rachitis are well handled by Edwin A. Locke and Isaac A. Abt respectively.

Volume III begins with diseases of the digestive tract. Of the numerous excellent articles that come under this heading none are more valuable than Louis Starr's timely discussion of diseases of the mouth, and Wilder Tileston's chapter on pancreatic disease. Diseases of the respiratory tract are next considered by such able writers as B. R. Shurly, Robert D. Rudolf, Allison Walter Hewett, George Blumer, and Joseph C. Capps, whose contributions leave nothing to be desired. The third section of this volume is devoted to diseases of the circulatory system. Pericarditis is considered by Alexander and William F. McPhedran, while all other circulatory diseases are taken up by Charles Spencer Williamson. The final section is given over to diseases of the blood and ductless glands. All the chapters on blood diseases are written by C. F. Martin, and Frederick Forchheimer, the editor, contributes the carefully prepared chapters on diseases of the adrenals, the spleen, and the thyroid and parathyroid glands.

In the last volume, Volume IV, diseases of the kidneys, diseases of the bladder, gonorrhea, and other diseases of the male sexual organs, nervous diseases, and diseases due to protozoa and the various tropical diseases are all considered. The management of nephritis and amyloid disease of the kidney is discussed by Joseph L. Miller, while the treatment of other kidney conditions has been left to the facile pen of Frank Sherman Meara. Genito-urinary conditions are well discussed by E. L. Keyes, Jr. Organic diseases of the nervous system have been written by Joseph Collins, Edwin G. Zabriskie, Howell T. Pershung, and John Grinker, while the neuroses are taken up by Lewellys F. Barker and Smith Ely Jelliffe. The various phases of tropical diseases are carefully considered by such well-qualified observers as William B. Wherry, Paul G. Woolley, and Creighton Wellman.

It is obvious that to attempt to discuss critically the vast and varied field covered by these volumes is well-nigh out of the question. The above brief sketch of their contents will at least convey some idea of the thoroughness with which the treatment of internal diseases has been covered and the eminence of the authors to whom this task has been intrusted. In all the contributions certain features are characteristic. The treatment of the various diseases is considered from all aspects, the practical bearing of anatomy, physiology, pathology, and chemistry on the management of diseased conditions is never lost sight of, the various forms of treatment are described in such detail that they may be easily carried out, and unusual emphasis is placed upon the newer forms of specific, hygienic, and mechanical methods of managing disease. The list of important references to the literature given at the end of most of the chapters is a valuable aid to all who may be interested from time to time in the investigation of certain of the subjects.

Too much praise cannot be bestowed upon the painstaking way in which all the volumes have been edited. As a result, they will stand not only as models of valuable works of reference, but what is even more desirable, they are destined to take a prominent place as useful books for the daily help of the practitioner.

G. M. P.

A TEXT-BOOK OF HISTOLOGY. ARRANGED UPON AN EMBRYOLOGICAL BASIS. By DR. FREDERIC T. LEWIS, Assistant Professor of Embryology at Harvard Medical School, and DR. PHILIP STÖHR, formerly Professor of Anatomy at the University of Würzburg. Second edition; 539 pages; 495 illustrations. Philadelphia: P. Blakiston's Son & Co., 1914.

IN this revised edition of Lewis' arrangement of Stöhr's *Histology*, over one-fifth of the illustrations are of an embryological character, and the book, as a whole, conforms in a high degree to the plan originally laid down by Professor Lewis. This plan was to present the development of each organ, or system of organs, before detailing the microscopic structure. That this is a valuable addition for a student of anatomy may be seen by examining the introduction to the study of the heart, digestive tube, or reproductive organs. Here are given in short form, with illustrations, a clear account of the changes which occur from the simple form of early embryonic life to the later definitive stages.

An important change from the previous edition is the insertion of references to original sources, not only to recent papers, but also to those authors who first gave a good account of the structures under discussion. Thus we have citations from Robert

Hooke (1664) on cells; Leeuwenhoek (1677) on spermatozoa; Vesalius (1604) on bloodvessels; Aselli (1622) on lymphatics, and many others. These are not given in lists at the ends of chapters, or as footnotes, but are worked into the text in an interesting and attractive way. The result is a stimulating book, which will serve not only to give information, but also to give the student a perspective of his subject, and to teach the discerning ones how to supplement their knowledge by further study. W. H. F. A.

THE BIOLOGY OF THE BLOOD CELLS. By O. C. GRUNER, M.D. (Lond.), Assistant Professor of Pathology, McGill University, Montreal. Pp. 392; 7 colored plates; 75 illustrations. New York: William Wood & Co., 1914.

THIS volume represents an extremely ambitious and complete collection of all the important hematological work that has appeared in the recent literature of the subject. The author has gathered together the various expositions of theories and demonstrations of facts that are in any way connected with the biology of the blood cells and placed them in a form that is readily accessible to those willing to delve into the complicated depth of the morphology, the genesis, the life history, and the functions of the various types of blood cells. It cannot be gainsaid that all this represents a tremendous amount of work; there are 644 separate and distinct references, but the value of such work, representing for the greater part a collection of literature, is certainly open to question. Whether or not such compilations are deserving of particular praise, aside from that which should be given to mechanical perfection of any kind, is very dubious.

The book consists of seven chapters, dealing respectively with primordial, red, lymphocytic, monocytic, neutrophilic, and phlogocytic forms of blood cells, and with the cytoplasmic phenomena of blood-forming tissues. Following this there is an appendix containing a list of the abbreviations employed, the references to the literature, and an extremely comprehensive glossary of hematological terms. Last of all are the indices, four in number, a general index, and indices of the diseases, the animals, and the authors referred to.

In reading the book several facts stand out with particular prominence. One is impressed by the intense admiration the author apparently feels for Pappenheim, as shown by the stress he lays upon his theories and ideas, frequently neglecting entirely the opinions of other hematologists, only somewhat less distinguished. One is also impressed by the utter futility of endeavoring

to use the work "as a companion to any of the larger text-books on hematology." The information is so abstruse and so complicated that it would require either a careful study of the book from the beginning to fully comprehend much that is written or else one would have to be a student of advanced hematology to follow the various statements and arguments.

Several criticisms more specific might be made. The author accepts the intermediate view of Pappenheim as to the origin of the blood cells, and seems to dismiss the pure dualistic theory without sufficient consideration. On page 66 no mention is made of the strong possibility of the nuclear body seen in human erythrocytes being an artefact. At times there is a tendency to contradict statements previously made, as with chlorosis and punctate basophilia on pages 79 and 81. Reading page 100, one receives a shock to find that "the ordinary blood-count is of relatively small value in elucidating the pathology of a case of anemia." On page 167 reference is made to Asher's work upon iron metabolism and the spleen, but the iron content of the feces was estimated, not that of the urine. Similar minor errors, for the most part unavoidable, are found from time to time in the latter pages. In considering the glossary of hematological terms exception might well be taken to even noticing some of the etymological monstrosities that the author has seen fit to include for the sake of completeness. Incidentally he here tabulates 86 synonyms for Pappenheim's lymphoidocyte.

The necessity of such a book as the present one may be questioned; there can be no question but that the subject matter is presented in a deeply scientific and scholarly fashion. The author has done well a difficult and imposing task. J. H. M., JR.

MASSAGE, MANUAL TREATMENT, REMEDIAL MOVEMENTS, HISTORY, MODE OF APPLICATIONS, AND EFFECTS; INDICATIONS AND CONTRA-INDICATIONS. By DOUGLAS GRAHAM, M.D., Consultant and Instructor in Massage, Boston, Massachusetts. With a Chapter on Massage of the Eye, by DR. A. DARIER, formerly President of the Ophthalmological Society of Paris; Chevalier of the Legion of Honor, etc. Fourth edition; pp. 574; 75 illustrations. Philadelphia and London: J. B. Lippincott Company, 1913.

THIS the fourth edition of "the first book on massage in point of time in the English language" appears as a well-bound, splendidly printed volume.

The revision has not been extensive, and certainly seems to fall

short of the possibilities of such a work eleven years after the appearance of its admirable predecessor. Twelve new illustrations, about forty paragraphs, and a chapter on massage of the eye constitute the additions. A few paragraphs have been omitted. The new paragraphs usually introduce or conclude the chapter as it appeared in the former edition, and touch upon the possibilities of massage in such conditions as angina pectoris, arteriosclerosis, atonic dilatation of the stomach, pneumonia, etc. Some few lines are devoted to Bier's hyperemia.

The author still feels that manipulation of the gall-bladder through the abdominal wall may aid in the solution of biliary calculi, and he seems to have little respect for the surgeon's viewpoint of appendicitis.

The book remains largely a record of the early personal experiences of a man who is intensely enthusiastic about his subject, but has allowed himself to be slightly overbalanced by it.

The chapter dealing with the mode of applying massage is excellent. The illustrations are very good. As a new edition it is somewhat of a disappointment; as a book on massage it remains an excellent treatise.

T. G. S.

MODERN RADIUM AND THORIUM THERAPY IN THE TREATMENT OF TUMORS, GOUT, RHEUMATIC DISEASES, NEURALGIAS, AND THE DISEASES OF THE BLOOD. By ADOLPH BICKEL, M.D., Professor in the University of Berlin. Pp. 40. Berlin: August Hirschwald, 1914.

THIS is a small monograph on the treatment of various conditions by radium and mesothorium. The author reviews briefly the physics of radio-active substances and radio-activity, the indications for the use of the two mentioned and their value, and gives a summary of cases he has treated.

H. K. P.

MODERN SURGERY. By JOHN CHALMERS DaCOSTA, M.D., LL.D., Professor Surgery, Jefferson Medical College, Philadelphia; Surgeon to Jefferson Medical College Hospital; Surgeon to St. Joseph's Hospital; Fellow of the American Surgical Society, etc. Seventh edition; Pp. 1515; 1085 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

THIS the seventh edition of the author's work has added much to his already valuable treatise on surgery. The book has been reset, and to keep the work in as small a compass as possible the

pages were made longer and wider, thus keeping the bulkiness at a minimum. An endeavor has been made to steer a mid-course between prolixity and brevity, to winnow the grain from the chaff of all that has been published in recent years as truths, and by giving opposing views, in some instances to allow the reader to choose.

Due credit is given every author for his work, and in many instances the original author's own description is quoted *verbatim*. Many statements of discoveries or findings are accompanied by the author's name and reference to the article, thus enabling easy reference to the original if so desired.

The subject has been brought as nearly up to the day as any work can be in this age of such rapid strides in surgery and its allied subjects. The chapters on laryngology are very good, containing the very latest and approved literature on tracheobronchoscopy and esophagoscopy.

The chapters on bacteriology, seriology, and radiography are well presented, and make very clear, instructive, and interesting reading.

The entire subject of surgery is well covered, in fact as completely as can be done in a one-volume book, although the reviewer ventures to suggest that more text space could have been used for descriptions of operations such as are seldom found outside an operative surgery. This space could have been obtained by omitting some of the illustrations of bacteriological slides, monstrous tumor specimens in the late stages, when a diagnosis is either useless or certain, or both.

Careful reading found several minor failings, such as an instance of faulty indexing, which is merely incorrect page quotation, one or two of the fracture dressings differ rather widely from the general use, but this is a matter of personal opinion and adaptability to individual cases.

On the whole the book is an excellent one, well illustrated, and up to date. It makes pleasant, easy, and very instructive reading. The vocabulary and style are typical of the author—excellent.

The work may well grace the shelf of either a surgeon or a student still in his undergraduate course.

E. L. E.

CLINICAL DISORDERS OF THE HEART-BEAT. By THOMAS LEWIS, M.D., F.R.C.P., Assistant Physician and Lecturer on Cardiac Pathology, University College Hospital. Second edition, pp. 116. London: Shaw & Sons, 1913.

THE prompt appearance of a second edition of this little book attests its popularity among medical men. This new edition

in no way differs from the earlier one except for the addition of a chapter upon auricular flutter. The author describes the nature of this rare cardiac disorder, discusses its etiological and pathological relations, details its symptomatology and mode of recognition, and outlines the course of treatment. The incorporation of this chapter brings the book fully up to the present-day knowledge of cardiac arrhythmias, making the book of great value to those sufficiently interested to desire a clear working knowledge of this interesting phase of disturbances of the heart.

J. H. M., JR.

A MANUAL OF ELEMENTARY ZOÖLOGY. By L. A. BORRADAILE, Lecturer in Zoölogy, University of Cambridge. Pp. 470; 301 illustrations. London: Henry Frowde, Oxford University Press.

THIS book, as the title indicates, is one of that large class of texts which aims to present the main facts of zoölogy without making any attempt to outline a method of teaching the subject. It departs somewhat from the exact type of manual indicated by devoting the first 108 pages to a detailed consideration of the frog. Following this the larger groups of animals are taken up in the order of their complexity and considered in much less detail. It is the apparent purpose of the author to give the main facts concerning the group, and this is done sometimes by the discussion of a single animal and sometimes of several. As a rule a single chapter is devoted to a Phylum but in some cases such material is distributed through a number of chapters. The Porifera, Echinodermata, the worms aside from the Annelida, and Reptilia are omitted. General subjects under the headings "Reproduction and Sex," "Embryology," "Classification and Evolution," "The Animal and the World" are discussed in separate chapters. The illustrations are numerous and generally good. Marginal references in bold faced type and italicized terms in the text are commendable features of a uniformly good typography.

There does not appear to be any good reason in the nature of this book why it should be added to the already overcrowded market. No conspicuous merit of subject matter or method characterizes it, while on the other hand there is a lack of balance, and not a little misinformation to be found. A better acquaintance with researches in countries other than his own would have served to keep the author from many mistakes. Indeed, the book is distinctively English throughout and has the strength as well as the weakness which characterizes the biological writings from that country. It will probably make its own individual appeal and find a place of usefulness, and if there is to be a multiplicity of books of one kind it has quite as much right to exist as many others.

C. E. M.

TREATMENT AFTER OPERATION. By WILLIAM TURNER, M.S., F.R.C.S., Senior Surgeon to the "Dreadnought" Seaman's Hospital Greenwich, etc., and E. ROCK CARLING, B.S., F.R.C.S., Surgeon to the "Dreadnought" Seaman's Hospital Greenwich, etc. Containing a chapter on the Eyes, by L. V. CARGILE, F.R.C.S., Senior Ophthalmic Surgeon and Lecturer on Ophthalmology, King's College Hospital, etc. Pp. 247; 55 illustrations. London: University of London Press.

As is indicated in its preface this work is especially valuable, to house surgeons, students, and nurses. The data is obtained entirely from the personal experience of the writers and no attempt has been made to elaborate theories or modifications of treatment.

The treatment is begun in the sickroom before operation and the patients followed through their convalescence, each symptom and sign demanding treatment being taken up and disposed of. In many minor points, the procedures used are not altogether approved by surgeons at large. Cracked ice for thirst is an atrocious practice. Drugs for postoperative vomiting are useless. More stress should be laid on the stomach tube.

Many of the illustrations are exceedingly well chosen, but several leave much to be desired in what they are intended to show.

In conclusion, I would commend the book as a fairly complete *resume* of after-treatment which will be of wonderful aid to surgeons of little experience as the authors state. E. L. E.

THE PEOPLE'S MEDICAL GUIDE. By JOHN GRIMSHAW, M.D., B.S. (Lond.), D.P.N. (Camb.), M.R.C.S. (Eng.), etc. Pp. 839; 112 illustrations. New York: Macmillan Co.

In scope this book is a veritable medical encyclopedia of such information as should be at the disposal of the public.

The sections devoted to the dietetics and hygiene of infancy and childhood are excellent in every way; their true import is lost, however, unless their relationship to the normal development of teeth, digestive tract, bones, and nervous system is appreciated. The author contends that a normal adult is an impossibility unless preceded by a normal child, and that a normal child is likewise impossible unless nature's laws are understood and followed. The onus of the situation thus falls on the parent and doctor to keep rather than get the child well.

Under infectious and contagious diseases the interests of the community were kept well to the fore. The public conscience is sharply prodded as regards reporting and quarantine as well as

regarding measures preventive to the spread of disease not generally considered as contagious.

The portion devoted to surgical conditions should dispel much of the present ignorance and dread of surgical procedures as such and should leave clearly in mind set conditions in which surgery holds the only hope of recovery.

Such broad questions as eugenics, venereal disease, and cancer are thoroughly discussed.

Much valuable material is found in the final sections on feeding and exercise. Not only are these of interest as applicable in diseased states but also in the daily business of keeping a healthy body well.

The author, in so far as the main object of his book is concerned, seems to have somewhat overshot the mark. His subtitle reads in part, "Points for the Patient, Notes for the Nurse, Matter for the Doctor." That these three types of information are found is true. To the doctor and nurse this will not prove confusing, but a patient might, at times, trespass on forbidden ground to his sorrow.

A. A. H.

THE MOSQUITO: ITS RELATION TO DISEASE AND ITS EXTERMINATION. ALVAH H. DOTY, M.D., formerly Health Officer of the Port of New York. Pp. 79; 10 illustrations. New York and London: D. Appleton & Company.

THIS little book, from the pen of one who is so well qualified to speak with authority on this subject, will find many readers. Simplicity and clearness, both in the text and illustrations form its keynote. This is especially fortunate as the problem of the mosquito, as the author insists, is one which can only be successfully approached by the united effort of all. A working knowledge is here obtainable presented in such a way as to be above the head of practically no one.

A. A. H.

THE DISEASES OF THE SKIN. BY WILMOT EVANS, M.D., B.S., B.Sc., F.R.C.S., Surgeon to the Royal Free Hospital, and Surgeon to the Skin Department, Royal Free Hospital; Senior Surgeon to the Hospital for Diseases of the Skin, Black Friars. Pp. 375; 32 illustrations. London: University of London Press.

THE author of this small volume which is intended as an introduction to the study of diseases of the skin, has succeeded remarkably well in the always difficult task of combining clearness of

description with great conciseness. While it is, of course, impossible to discuss with any degree of detail the various diseases of the skin within the limits of such a manual, yet the essentials of the subject are well covered. The author's views are in the main those commonly held, but in a few instances they are somewhat at variance with usually accepted ones. Ecthyma is regarded as simply a variety of impetigo contagiosa, an opinion which scarcely seems to be in accord with clinical facts. Herpes labialis, especially that variety associated with other diseases, is thought to be due to the organism causing the affection with which it is associated; *e. g.*, the herpes of pneumonia is looked upon as the direct effect of the pneumococcus upon the mucous membrane of the lip, the author having found, as he believes, this organism in the vesicles. Vitiligo is thought to be probably the result of some toxin having its origin in the alimentary canal.

We learn with some surprise that the primrose (*Primula obconica*) is the most frequent cause of plant dermatitis in England.

The book is a very good one of its class, and will be found useful by the student, but it cannot, and is not intended to, take the place of larger and more formal treatises on diseases of the skin.

M. B. H.

PROMPT AID TO THE INJURED. By ALVAH H. DOTY, M.D., Late Health Officer of the Port of New York. Fifth edition. Pp. 229; 85 illustrations. New York and London: D. Appleton & Company.

THIS book, meeting, as it has in the past, the broad need of a guide in accidents of all kinds, has become more than ever valuable since this latest edition has been brought abreast of the latest knowledge in surgery, medicine, and sanitation.

While its possession will come amiss to no one, its greatest field of usefulness will be found, as of old, where the community masses itself in factories, camps, and similar places; that is, where accidents most frequently occur.

A. A. H.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Wassermann Reaction and its Application to Neurology.—FILDES and McINTOSH (*Brain*, xxxvi, part ii, 193), maintaining that the mere report of a Wassermann reaction is of little value unless one knows the technique used in securing it, describe at some length the methods employed by them in the study of many neurological conditions. It is interesting that, as a result of careful studies, they have come to use, as an antigen, a cholesterinized alcoholic extract of fresh human heart. The advantages claimed are the great invariability of such antigens, and the fact that they give a much higher percentage of results in undoubted lues, while at the same time they manifest no tendency toward non-specificity findings quite in accord with those reported by Walker and Smith, Kolmer and others. They find that inactivation of sera causes a reduction in the amount of the reacting substances much greater than that observed in inactivated spinal fluids. The preliminary titrations, and dilutions are clearly explained. Their findings in the various stages of syphilis in general accord with those already reported: these in brief are: (1) The reaction is negative in non-syphilitic diseases of the central nervous system. (2) The occurrence of a positive reaction in the spinal fluid is indisputable evidence of a luetic infection. (3) The reaction in cerebrospinal lues varies much according to the location of the process, being inconstant, weak, or negative except when the spinal cord itself is involved, in which case the reaction is remarkably strong. Moreover in this group of cases they find position reaction more often in cases showing recent lesions. (4) In general paresis a strong reaction is nearly always present in both serum and spinal fluid, the same being true of tabes

unless examined after the disease has existed for some time or has been well treated. (5) So common is the occurrence of a positive reaction in the spinal fluid and a negative one in the serum, and *vice versa*, that the negative finding of one alone is insufficient evidence to exclude a luetic process. As regards the results of specific therapy the authors call particular attention to the fact that some cases of paresis and tabes should not be grouped as "true parasymphilitics," since some are really active cases of lues. They find indeed that the best therapeutic results are secured in those cases in which there is evidence of active meningeal involvement, cases which they regard as transition forms between true dementia paralytica and cerebrospinal syphilis. Treatment has little or no effect upon the Wassermann reaction in pure parasymphilitic cases, a result so different from that seen in cerebrospinal lues as to be of real value in a prognostic sense. It would seem that the rapidity with which a positive spinal fluid can be reduced to a negative state bears little relation to the duration of the infection; this is the reverse in the serum in which the chronicity of the disease varies directly with the speed of change of the reaction. The authors are of the opinion that the "salvarsan-provocative test" has been given an exaggerated diagnostic value.

The Pathological Excretion of Amino-acids.—LOBBE and BITH (*Arch. des malad. de Pappar. dig. et de la nutrit.*, vii, p. 681 to 688), have used a method modified from that of Jäger, in which 40 c.c. of urine are mixed with 10 c.c. of 5 per cent. magnesium hydrate and a few drops of phenolphthalein. After a few moments the solution takes on a rose-red color, showing that the acid of the urine has been neutralized. One now adds 10 c.c. of 10 per cent. sodium phosphate, allows the mixture to stand from two to three hours, and then filters. 15 c.c. of this filtrate are neutralized with one-fourth normal sulphuric acid, and after the addition of 5 c.c. of neutralized formol the resulting acidity is estimated, using one-tenth normal sodium hydroxide, 1 c.c. of which equals 0.0014 gm. of amino-acid nitrogen. Increased amino-acid excretion occurs in insufficient amino-acid destruction on the part of the liver, in cases where pathological destruction of proteids is going on, and third, in conditions of acidosis, whether diabetic or of another nature. Of 40 cases of hepatic disease, all cases which showed a marked injury to the tissues showed an equally marked increase of amino-acid in the urine. Normal values occur in uncomplicated gall-stones and catarrhal jaundice. The same is true in the cases of early Laennec's cirrhosis, but in the later stages of the disease the excretion is increased. Abnormally high values also occur in fatty degeneration, cases of primary tumor, cirrhosis secondary to cardiac disease, and in cases of phosphorus and chloroform poisoning. In cases of marked diabetic acidosis, values of from 0.92 to 3.04 gm. of amino-acid nitrogen per day were found, these values representing 8.4 to 18.4 of the total nitrogen output. In a number of diseases of the gastro-intestinal tract, in gout and chronic rheumatism, normal values were found. In those acute and chronic diseases which are accompanied by an abnormal breaking down of protein tissue, such as occur in the late stages of typhoid, in the crisis of pneumonia and during the absorption of pleuritic and other exudates, in leukemia, etc., constant increased

amino-acid excretion was observed in the urine. As a functional test, designed to show the inability of the liver to perform its normal amino-acid decomposition, Lobbe and Bith recommend the administration of 20 gm. of pepton while the patient is on a simple milk diet. If under these conditions an increased amino-acid excretion is observed, in all probability this indicates an affection of the liver.

Sulphemoglobinemia.—R. L. M. WALLIS (*Quart. Jour. of Med.*, vii 73 to 91) gives an historical review of the literature on the subject of sulphemoglobinemia, bringing together a total of 5 cases, including 3 observed personally. He further presents a clear *resume* of the chemistry and spectroscopic tests for this substance in the blood. All the cases present a fairly characteristic clinical picture dominated by the presence of extreme cyanosis, weakness, headache, and constipation, without dyspnea, heart disease, or alteration in the red-blood count. The diagnosis may be easily made by the spectroscopic examination of the blood or even of the lobe of the ear. The urine in these cases is apt to be extremely dark. As a special finding the author notes the occurrence in the saliva of nitrite-forming bacteria, which have been readily secured in pure culture and are easily grown on most media at a temperature of about 25° C. These bacteria apparently produce their nitrites from the amino-acids of the blood and impart to the latter a reducing substance, the exact nature of which is not yet known though it is probably a hydroxylamine derivative. This substance, according to the author, caused a partial reduction of oxyhemoglobin, which is subsequently converted into sulphemoglobin by the hydrogen sulphide arising from the intestinal tract. The author made some attempts at vaccine therapy, using the nitrite bacillus, but with doubtful results. Careful regulation of the intestinal movements has some influence upon the condition, but like oxygen inhalations only of a transient nature.

Complement-deviation in Graves' Disease.—ROSEO (*Il Poli-clinico*, xx, 1249 to 1251). In a previous communication Roseo showed that the sera of 4 out of 5 cases of typical exophthalmic goitre gave complete complement fixation with each of two aqueous antigens made from thyroid tissue removed at operation. The sera from cases of the so-called "formes frustes" gave negative reactions with the same antigens, while the sera from 13 normal people and those from 5 cases of lues, which were confirmed by the Wassermann reaction, also gave negative results. Since reporting this first series in 1912 the author has continued the test, running the sera parallel with the Wassermann reaction in order to see if the above fixation is a specific phenomenon or one due to some factors common to both goitre and lues. He has secured complete fixation in 4 cases of true Graves' disease and negative results in 3 mild cases and in 2 patients suffering with thyroid adenomas. In only 1 of the above cases was there a positive Wassermann, but in this instance a previous luetic infection was admitted. These reports are rather in accord with the work reported by Papazoula, who secured 58 positive reactions out of 60 cases investigated. Papazoula also secured negative results when testing control sera with the Basedow antigens. Roseo further reports the examination

of sera of four patients after removal of the thyroid gland. In two of these there was marked postoperative clinical improvement, and the test became negative within fifteen to thirty days after operation. The author advances some hypotheses as to the nature of the reaction, but admits that the evidence at present is far too meager to permit of any definite conclusions.

SURGERY

UNDER THE CHARGE OF

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Valve Formation in the Urinary Bladder for the Escape of Ascitic Fluid.—ROSENSTEIN (*Zentralbl. f. Chir.*, 1914, xli, 373) conceived and put into practice the idea of permitting the ascites, due to liver cirrhosis, to escape into the urinary bladder. A woman, aged sixty-two years, suffered from liver cirrhosis and ascites since 1911. Rosenstein made an anastomosis between the portal vein and the inferior cava, *i. e.*, an Eck fistula. Unfortunately the success was only temporary. Later he did a Talma operation (suturing the spleen and great omentum to the abdominal wall and painting the surface of the liver with tincture of iodine), but this was also unsuccessful. In June, 1913, he did the following operation: The abdomen was opened freely and the whole peritoneal covered portion of the bladder exposed. He then drew a portion of the summit of the bladder through a silver ring, 3 cm. in diameter, cut the apex of this portion of the bladder with a scissors, and turned the margins over the ring all around so that the serosa was applied to serosa and fixed it in this position by silk sutures. This gave a free communication between the bladder and peritoneal cavity. He then excised a strip of the serosa and muscularis of the bladder wall all around below the ring and silk sutures, leaving only the mucosa. The upper and lower margins of this raw surface were sutured together, muscularis to muscularis and serosa to serosa. This forced the mucosa layer inward in the form of a circular double layer which, when the bladder was allowed to drop into place, acted as a valve to prevent the escape of urine into the peritoneal cavity. But it permitted the ascitic fluid to make its way into the bladder. The operation also provided against leaving any sutures in the mucosa, which is important in all bladder operations. The abdominal wound was closed, primary healing occurred, and after a short time the patient left her

bed. The ascitic fluid passed out with the urine, and the cystoscope showed that the valve functionated perfectly. The cure was not complete, as the ascitic fluid had to be withdrawn by puncture about every eight weeks, whereas before the first operation it was done about every eight days.

Thirteen Years' Experience with Pyloroplasty.—FINNEY and FRIEDENWALD (*Surg. Gyn. and Obst.*, 1914, xviii, 273) present their results with this operation, which Finney introduced in 1902, and a discussion of its advantages and disadvantages. The records of 100 cases, in which the operation was done, were studied. Of the 100 cases, the final results in 17 are unknown, while 5 died soon after operation, leaving 78 cases, in which the average percentage of favorable satisfactory recoveries was 93.8 per cent., the later deaths, 5 per cent., or favorable results 88.8 per cent. The operation has its greatest indication in the relief of pyloric stenosis, due to chronic ulcers, situated at or near the pylorus, and on either side of it or resulting from cicatricial contraction following the healing of such ulcers. It is often a useful procedure in cases of hemorrhage due to gastric ulcers on the lesser curvature or to duodenal ulcers which cannot be controlled medically, and which threaten the life of the patient, as well as in the chronic dyspepsias due to ulcers which have not been relieved by medical treatment. The operation has certain advantages over gastro-enterostomy and few of its disadvantages. Such objections as are advanced against the operation, *e. g.*, its inapplicability in the presence of active and bleeding ulcers, and also because of the fact that the new opening is not at its lowest point, taking advantage of gravity, are, according to their experience, more fanciful than real, since the operation has frequently been performed under these circumstances with most gratifying results. The interesting experimental work of Cannon and Blake and others supports this contention. The only contra-indications to the operation are inability to mobilize the duodenum when adhesions are too dense, and thickening and infiltration about the pylorus due to hypertrophic forms of ulceration. These are rare, however. In atony or gastropptosis with slight motor insufficiency such as observed in the water-trap stomach, or in nervous dyspepsia, *i. e.*, in gastric disturbances not dependent upon organic disease, this operation is contra-indicated. The special advantages lie in its affording the opportunity to excise all ulcers in the anterior walls of the stomach or duodenum after direct inspection of the part affected; also the application of treatment to ulcers situated in the posterior walls. It does not greatly disturb the normal relation between the stomach and intestines, as is the case in other operations. From their experience the immediate as well as the final results are most encouraging, while in some instances partial gastrectomy or gastro-enterostomy is undoubtedly the operation of choice; nevertheless, on account of its simplicity and satisfactory end results, they believe that pyloroplasty will continue to retain its position as a safe and useful procedure.

The Direct Implantation of Nerves into Muscles.—HEINEKE (*Zentralbl. f. Chir.*, 1914, xli, 465) experimented on the hind legs of rabbits. The two branches of the sciatic nerve, the internal and the external

popliteal nerves, were exposed in the thigh and a piece of the internal, 1 to 2 cm. long, was excised. The posterior muscles of the leg were thus paralyzed completely. The external popliteal or peroneal nerve was then followed outward and downward and divided below the head of the fibula. Finally a small channel was made through the gastrocnemius in a suitable place by a blunt instrument. The proximal end of the peroneal nerve was then passed through this channel and fixed in position by suturing over it a small muscle fold. Fourteen days later mild responses in the gastrocnemius were obtained by faradic and galvanic irritation of the peroneal nerve. After four weeks the whole prominence of the gastrocnemius reacted with strong contractions. After eight weeks the strength and extent of the contractions could not be distinguished from the normal, and not only did the muscle contract in which the nerve was implanted, but the neighboring muscles of the flexor group as well. At this time the muscles, which in the beginning were wasted and yellow, had recovered completely their normal color and consistency. Heineke has also shown that a muscle deprived of its nerve supply for twenty-one days, from the implantation of a sound nerve, can recover its function.

A New Method for the After-treatment of Prostatectomy.—VAN BISSELIK (*Zentralbl. f. Chir.*, 1914, xli, 503) says that the method makes use of a permanent catheter for a few days after the operation, so that only a small opening in the bladder wall is necessary through which a tampon is brought out. After the removal of the prostate in the usual way the wound and, if the hemorrhage is severe, the whole bladder are tamponned with gauze. The catheter, which was used before the operation to irrigate and empty the bladder, is left in position in the bladder. The greater part of the bladder wound is closed in two layers, catgut for the mucous membrane and silk for the outer layer. The part of the bladder wound remaining open is enclosed with a purse-string suture of catgut, which is passed from the outer side to the muscularis, but is not left long. The space of Retzius is tamponed and the abdominal wound is closed around the bladder tampon. Usually this is removed in twenty-four hours. The bladder is then washed out from above and below and the bladder wound is closed by inversion of its edges and tying the purse-string suture. A tampon down to the closed bladder wound will provide for the escape of any urine that will escape later. The bladder is washed out every two hours and the catheter changed every day. This continues for three or four days. Then it is left out at night for seven or eight days. After that the patient can urinate spontaneously at night. Six of the nine cases operated on in this way urinated spontaneously within fourteen days. The three remaining cases had cancer of the bladder.

Bimanual Examination of the Prostate.—HABERLAND (*Zentralbl. f. Chir.*, 1914, xli, 675) finds the bimanual method of examination very satisfactory. Since the anterior surface of the prostate lies behind the lower portion of the symphysis pubis, the finger reaches it when introduced into the rectum only 4 to 6 cm. from the external sphincter, while the finger of the other hand can be pressed downward against

the empty bladder and abdominal wall and thus against the prostate as in examining the uterus in the female. Even with a thick, tense abdominal wall, the method will rarely fail. Haberland has proven the correctness of his diagnosis by prostatectomy. By practice, one can determine the size and form of the seminal vesicles and vasa deferentia. By this method, the diagnosis can be made between vesical calculus and hypertrophied prostate. Only in isolated cases will it be necessary to invoke the aid of the x-rays, for more certainty in the differential diagnosis between these two conditions. The patient lies on his back with the knees drawn up and breathing through his mouth. The bladder is first completely emptied, voluntarily or by catheter. Fecal masses in the rectum do not disturb the examination.

THERAPEUTICS

UNDER THE CHARGE OF

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The Emetin Treatment of Amebic Dysentery.—YEOMAN (*New York Med. Jour.*, 1914, xcix, 327) reports 7 cases of amebic dysentery treated by subcutaneous injections of emetin hydrochloride. The disease varied in duration before treatment with emetin from six months to fourteen years. Other forms of treatment, including ipecac in 4 cases, had been employed in all the patients, with temporary benefit only, 5 patients were cured clinically, 2 were greatly improved, and none died. One of the "cured" cases recurred five months later. The average dose of emetin hydrochloride is one-half grain dissolved in 10 to 15 minims of salt solution and injected subcutaneously in the region over the deltoid. The remedy should be given until the symptoms disappear, and then the administration of emetin should be discontinued, for an excessive amount of emetin frequently produces marked bowel irritation. Yeoman believes emetin is specific for amebic dysentery in the same sense that quinine is specific for malaria or salvarsan for syphilis. When it is used early in the disease, cure should be prompt and permanent in all cases. Naturally when the amebæ have invaded the tissues deeply and are widely disseminated, cure may be permanent or clinical only. After weeks, months, or years encysted amebæ may reappear in an active vegetative form, accompanied by all the symptoms of an acute attack. Hence amebic patients should be kept under prolonged observation, and at the first signs of recurrence a course of emetin should be given. Because of the extensive destruction of the mucosa and the secondary infection of the ulcers, mucus, pus and blood in diminishing quantities may continue to be evacuated for sometime after all amebæ have disappeared from the stools. Irrigations and topical applications through the proctoscope will materially hasten the process of tissue repair.

The Magnesium Treatment of Tetanus.—STADLER (*Berlin. klin. Woch.*, 1914, li, 15 and 109), reviews the evidence of many observers on both the magnesium and phenol treatment of tetanus, and includes tabulated results of the different methods of treating tetanus. The results of the magnesium treatment compare very unfavorably with the results of Bacelli's method in the hands of the Italians. French, English, and Russian surgeons have also obtained excellent results with Bacelli's method, which is in contrast with the unfavorable results reported by German surgeons. Stadler says that at the present time it is impossible to judge of the relative advantages of the two methods. In general, he believes that phenol is more efficacious than magnesium, but if magnesium is given subcutaneously instead of intraspinally the difference is not so great. He is of the opinion that both methods add to the percentage of cures, but especially when they are combined with the serum treatment. He emphasizes the fact that more experimental and clinical evidence is necessary in order to determine which is superior. The article is very comprehensive, and reviews the literature of the subject in great detail.

Treatment of Tetanus by the "Rational" Method of Ashhurst and John.—BREM (*Jour. Amer. Med. Assoc.*, 1914, lxii, 191) quotes Ashhurst and John, who believe that the rational use of tetanus antitoxin consists in the intraneural injection of antitoxin; the intraspinal injection; the intravenous injection, and the infiltration of the tissues about the site of the injury. The quantity used should be very much greater than the quantity that has usually been given heretofore by the subcutaneous route. They have administered as much as 224,000 units during a period of three days. These authors feel that the outlook for patients with tetanus is much brighter since the development of this method of administering antitoxin, and that the old view, that antitoxin is of no avail after the symptoms of tetanus have developed must be abandoned. Brem reports a case of tetanus, treated along the lines suggested by Ashhurst and John, with very rapid recovery. This patient received a total of 98,000 units of antitoxin.

Serum Therapy in Scarlet Fever.—MOOG (*Therap. Monatsheft*, 1914, xxviii, 37) reports 25 cases of scarlet fever treated by intravenous injections of normal serum. The results obtained were very similar to those obtained by other observers with the use of serum from scarlet fever convalescents. The most striking effect obtained was a critical drop in the temperature, which begins in two to four hours after the injection and reaches its maximum in from eleven to sixteen hours. In addition to this drop in temperature is a corresponding favorable influence upon the toxic symptoms. The best effects obtained were in the severe uncomplicated toxic cases. Septic complications of scarlet fever were not influenced by this method of treatment. The author believes that the benefit ascribed to antistreptococcus serum in some cases to probably due to the effect of the serum alone. The injections should be made as early as possible in the course of the disease and not less than 80 or 100 c.c. of serum should be injected at one dose for children and 100 to 180 c.c. for adults.

Behring's Diphtheria Vaccine.—KISSLING (*Deutsch. med. Woch.*, 1913, xxxix, 2500), immunized 310 children following Behring's new method of combining the principles of both active and passive immunization. These children were exposed to an unusually virulent epidemic of diphtheria. Of 111 children who received two prophylactic injections none contracted diphtheria; of the remaining 119 cases receiving only a single injection 8 developed diphtheria. These 8 children were convalescing from scarlet fever and developed the disease in a mild form. Since the process of immunization requires several days it is possible that the disease developed in these cases before the time required to develop the immunity against the disease had elapsed. Kissling is convinced of the efficacy of this new method of immunization, and believes that it is far superior to the *older* method.

Some Theoretical Considerations Regarding Splenectomy in Pernicious Anemia.—EPPINGER (*Berlin. klin. Woch.*, 1913, I, 2409) advances a theory to explain the beneficial effect of splenectomy in pernicious anemia. He believes that the red-blood cells are destroyed in abnormal numbers in the spleen in pernicious anemia due to anatomical changes in the bloodvessels of the spleen. These changes allow large numbers of red-blood cells to enter the splenic pulp, where they are destroyed; the condition is essentially that of the pernicious anemia following hemorrhage, the patient bleeding into his own spleen. Eppinger found certain histological changes in the spleens of seven patients he removed that seem to support this view. He suggests that where the spleen cannot be removed, possibly ligation of the splenic artery might answer the same purpose. Eppinger also calls attention to the presence of "blood-lymph-nodes," that often are found in great numbers in cases of pernicious anemia. They seem to be similar to splenic tissue in their structure, and he suggests that when splenectomy does not benefit in pernicious anemia that these blood-lymph-nodes may be able to carry on the blood-destroying action of the spleen.

PEDIATRICS

UNDER THE CHARGE OF

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Hemorrhagic Disease of the Newborn and Direct Transfusion of Blood.—V. D. LESPINASSE (*Jour. Amer. Med. Assoc.*, 1914, lxii, 1866) gives as the chief causes of hemorrhagic disease in the newborn, syphilis, infection, hypoplasia of the coagulating elements of the blood, and asphyxia. Obstetrical complications and chloroform are of minor importance. According to Holt, syphilis is a causative factor in only 2 per cent. to 6 per cent. of the cases. The chief pathological lesions are the same as the clinical lesions, namely, hemorrhage and its conse-

quent anemia. The symptomatology is striking. Occasionally premonitory signs, such as restlessness, refusal to nurse, and slight elevation of temperature, are present. The chief symptom is spontaneous hemorrhage, and its site may be from the intestines, stomach, mouth, nose, ecchymoses of skin, pressure points of body, meninges, genitourinary tract, and eyes. Progressive pallor of the skin, gradual drying up of the tissues, weakening pulse, coma, and death follow a persistent hemorrhage. A black, tar-colored mass, with a pink fringe, seen in the stool, indicates hemorrhage in the gastro-intestinal tract. The treatment is the same whether the case is one of hemorrhagic disease of the newborn, Winkel's disease, Buhl's disease, jaundice with hemorrhage or hemophilia. The hemorrhage usually appears from the second to the fifth day of life; the earlier the onset the more grave the prognosis. In half the fatal cases death occurs suddenly within twenty-four hours or less. This is especially true in hemorrhages from the gastro-intestinal tract. The shortest clinical course observed by Lespinasse was four hours. A hemorrhage of one ounce in a newborn baby is equivalent to one quart in an adult. The three indications in the treatment are to stop the bleeding, replace the lost blood, and overcome the infection. Transfusion of live non-clotted blood meets all these indications in an ideal manner. This method will cure in practically every case, and it is never too late to transfuse if there is still the slightest auricular beat. Bowel cases should be transfused early. In Lespinasse's series of fourteen cases there have been no deaths from hemorrhage. The cessation of bleeding and the improvement in the general condition are simultaneous with the transfusion.

Juvenile Paresis and Salvarsanized Serum.—C. EUGENE RIGGS (*Jour. Amer. Med. Assoc.*, 1914, lxii, 1888) reports a case of juvenile paresis treated by the intraspinal injection of salvarsanized serum. The symptoms of juvenile paresis differ in no way, clinically or pathologically, from those of the generally recognized type. In either congenital or acquired syphilis the symptoms are due to the action of the *Spirocheta pallida* on the brain cortex. About one-half the cases develop after adolescence. It may occur in the very young, showing itself in mental retardation or feeble-mindedness. Fennell claims that 5 per cent. of imbecile children are congenital general paretics. Optic atrophy is an early symptom. Riggs reports the case of a boy, aged eight years, whose father had syphilis and gave a positive Wassermann reaction. Of the three other children in the family one gave a positive and two gave a negative reaction. The mental deterioration began in the boy's fourth year. At eight years the boy showed Argyll-Robertson pupils, exaggerated knee-jerks, ankle-clonus, and Babinski reflex in both feet, and marked Rombergism. There were no signs of congenital syphilis. The boy received eight intravenous injections of 0.25 gm. salvarsan followed next day by an intraspinal injection of 30 c.c. of a 40 per cent. solution of salvarsanized serum. The result was a return to normal pressure in the spinal fluid and a less positive blood-serum reaction. The other serobiological tests remained the same. But clinically, a marked improvement was noted, as the boy again fed himself, his vacuous expression disappeared, he became brighter mentally, and his gait improved.

OBSTETRICS

UNDER THE CHARGE OF

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Inversion of the Uterus.—BECKMANN (*Zent. f. Gyn.*, 1914, No. 18) reports the case of a woman in very weak condition, through repeated hemorrhage from an inverted uterus. This resulted from spontaneous birth under the care of a midwife. The patient was admitted to hospital, the abdomen opened by vaginal incision, the posterior wall of the uterus incised to the fundus, and the uterus reinverted. The tissues were then closed by suture and the uterus replaced in the abdominal cavity. The closure of the posterior vaginal wall completed the operation. The patient's recovery was complicated by infection without symptoms of peritonitis. The posterior cul-de-sac was opened and seropurulent fluid, containing abundant streptococci, was discharged. A drainage tube was inserted and the cavity of the uterus disinfected with tincture of iodine. The patient died of septic infection two days later. The second patient was subjected to colpeuryesis for seven days without result. Operation was then undertaken and the uterus replaced. Infection followed and drainage and the use of iodine were then employed. The patient made a tedious recovery. These cases emphasize the danger of infection and seriously raise the question whether in cases where infection has persisted long it is not better to extirpate the uterus.

Clinical Manifestations of Congenital Syphilis.—ARMSTRONG (*British Med. Jour.*, May 2, 1914) believes from clinical observation that while cases of congenital syphilis are becoming more frequent the severity of the disease is decreasing. Necrosis of the bones does not appear so often, but syphilitic disease of the nervous system, congenital in infants, seems to be on the increase. Improvement in diagnosis results in recognizing many cases which otherwise would have passed unnoticed. While the Wassermann reaction is reliable in the majority of cases the luetin test is better. In pregnancy the Wassermann reaction from the mother's blood is valuable and suggestive. In marasmic children the Wassermann test is often negative. Ten per cent. of pregnancies in syphilitic women result in the death of offspring before the end of the first year of life. The percentage of abortions is very large. In some cases repeated abortion is followed by the birth of a monstrosity. With the syphilitic rash may be confused pemphigus of the newborn. A true pemphigus is the result of a streptococcus infection of the skin. A syphilitic eruption with blebs is rarely found in newborn infants; when present it is on the palms and soles and is soon followed by the raw-ham color. Pemphigus occurs after birth and is not limited to the palms and soles. The syphilitic child is badly nourished; the infant with pemphigus may be well nourished. Eczema

affecting the scalp may be confused with congenital syphilis. In the former the eruption is scaly, greasy, and yellow on the scalp and folds in the face and behind the ears. When this occurs about the nates and is complicated with lack of cleanliness, inflammation and oozing may develop, which resembles syphilis. Gangrene occurring in a newborn child may be the result of syphilis, and a therapeutic test would clear up the diagnosis. After the first few years of life, children born syphilitic show the disease most often in laryngitis and warts. The latter are easily seen and cured. The laryngitis is chronic with acute attacks, and syphilis may not be suspected as a cause. Here a therapeutic test makes a diagnosis possible. Congenital syphilis may cause a discharge of blood in the urine. In these cases edema is usually a prominent symptom, and if autopsy is obtained the kidneys, on microscopic examination, show characteristic changes. In diseases of the nervous system, infants born with marked evidence of syphilis usually die early, those apparently healthy developing defects at the time of the second dentition or puberty and often develop paralysis. In other cases mental deficiency, imbecility, and idiocy may be present without physical sign of syphilis. In these the Wassermann reaction make the diagnosis. Meningitis in these cases is often basal, and while the child may not die it is usually permanently damaged. Syphilitic infants often become hemiplegic, and when this develops suddenly its occurrence is suspicious. Syphilitic children occasionally develop locomotor ataxia which is usually incurable.

Cesarean Section for Heart Disease.—BARRIS (*Jour. of Obs. and Gyn. British Empire*, April, 1914) reports the case of a multipara, with a history of rheumatism, who passed through a tenth labor without signs of cardiac failure. When admitted to the maternity department of St. Bartholomew's Hospital she was in a critical condition, the urine albuminous, the heart greatly dilated, with double aortic and mitral disease. An electrocardiogram showed extensive disease of the heart muscle. Although the child was not viable the mother's condition was so grave that pregnancy must immediately be ended. It seemed also best to sterilize the patient. Accordingly, stovain with dextrose dissolved in sterilized water was injected between the third and fourth lumbar vertebrae. A second injection was necessary, followed by full anesthesia. The patient's face was screened, so that she could not witness what was done. The operation was performed in the usual manner, and oxygen was administered and 1 c.c. pituitary extract. The patient felt no pain and blood-pressure, which at first was 240 mm. Hg., fell to 160. The pulse was from 90 to 55, then 75. Anesthesia lasted one hour, and a sandbag was placed on the abdomen to maintain intra-abdominal pressure. The uterus contracted well without hemorrhage, and the mother did well. Barris also has collected a report of a case done by Watts, under spinal anesthesia for mitral stenosis and kidney disease, at eight months pregnancy. The mother did well and the child was born alive. Wyatt operated at St. Thomas' Hospital under spinal anesthesia, tropococain with adrenalin, with delivery of a living child. The patient vomited during the operation. She died on the fifth day from cardiac failure. Stabb operated at Queen Charlotte's Hospital, using stovain and giving gas and

oxygen, a living child being born, which died nine days later from bronchopneumonia. The mother recovered. Under the conditions present this method seems clearly indicated.

Influence of Ectopic Pregnancy on the Uterus.—SAMPSON (*Surgery, Gyn., Obs.*, May, 1914), from an extensive study of the subject, finds that in early ectopic pregnancy the uterus increases in size by hyperemia of its muscle and thickening of its lining membrane. In the latter the changes are similar to those found in the decidua vera of early uterine pregnancy. The uterine wall shows arterial and venous hyperemia. The uterus contracts when the pregnant tube endeavors to expel its contents. These contractions lessen the arterial supply and damage the endometrium, causing outflow of blood. When tubal pregnancy ends the uterus undergoes involution: (1) by destroying recently developed tissue, and (2) by reconstructing new and normal tissue. The first takes place by free hemorrhage from the endometrium, with destruction of cells and filling of venous spaces. In the tube a similar process goes on, so that chorionic villi may remain in active condition in the tube indefinitely.

Retained Portions of Placenta; Their Significance and Management.—WINTER (*Monats. f. Geb. u. Gyn.*, 1914, Bd. 39, Hft. 5), contrary to much accepted belief, considers that retained portions of the placenta, in many cases, cause no disturbance whatever. He believes that symptoms developing in these cases were caused by local endometritis, or by infection at the placental site, developing in the conduct of labor. Instead of adding to the severity of infection in these cases, his observations led him to think that retained portions of placenta may actually make infection less severe. He is against the common practice of, in all cases where fever occurs, exploring the uterus for retained placental fragments. Under antiseptic precautions this can be done without causing fever in one-third of the cases; while in from one-half to two-thirds, reaction more or less severe occurs, and in 7 to 9 per cent. death follows. Infection by hemolytic streptococci seems to be the cause of the fatal result. The spontaneous expulsion of portions of placenta is without danger, and usually terminates fever which may be present. Infection in these cases does not enter the connective tissue of the uterus nor its blood-current, and hence recovery is rapid. So far as treatment is concerned he would not interfere with the uterus, because a portion of placenta was retained, unless hemorrhage occurred. When at the moment of labor the placenta does not completely come away, retained portions should be immediately removed. During the puerperal period, in cases without fever, where it is known that a portion of placenta is retained, this should be removed. When fever is present in the puerperal period, accompanied by hemorrhage and retention of a portion of placenta, the placental fragments must be removed. When there is no hemorrhage, but where placental polyp is present in the cervix or extending into the vagina, one should wait for spontaneous expulsion, helping it by the administration of ergot. Should this not succeed, bacteriological examination of the lochia should be made, and if the less virulent ferments or bacteria are present the uterus should be immediately cleared out. If virulent bacteria, as

streptococci are present, this should not be done, and one should wait for spontaneous expulsion of fragments or until pathogenic bacteria have disappeared. When it is evident that the peritoneum, parametria or adnexa are involved, active interference is contra-indicated. Active hemorrhage only would be a cause for operation. When it is decided to remove placental fragments, it should be done by the finger and not by a curette.

GYNECOLOGY

UNDER THE CHARGE OF

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Ovarian Transplantation.—The question of reimplanting into some portion of the patient's body one or both ovaries, or a portion of them, in order to prevent the various nervous sequelæ which so often follow an abrupt, surgical menopause, has interested surgeons for many years. This procedure comes into consideration of course only in cases in which, owing to the presence of advanced inflammatory or other changes, a truly conservative type of operation is impossible, and both ovaries must be removed. It having been pretty definitely proven that no type of heteroplastic transplantation offers the slightest hope of success, attention in recent years has been directed toward the reimplantation, as has been said, of the patient's own ovarian tissue, after freeing this from surrounding diseased structures. The chief experimenters along these lines at present are the French surgeons, especially TUFFIER, but a recent report from one of the French clinics by DE ROUVILLE (*Arch. mens. d'obst. et de gyn.*, 1914, iii, 161) is decidedly discouraging, and does much to justify the marked skepticism with which the procedure is viewed by the majority of American operators. De Rouville reports the results in nine cases of autoplasmic ovarian grafting, performed in conjunction with operations for various inflammatory conditions of the genital organs. In each case one or both ovaries was implanted beneath the skin of the abdominal wall, just to one side of the line of incision. *Anatomic Results:* So far as could be determined from subsequent abdominal palpation, the implanted ovary or ovaries underwent complete disappearance in four cases, and showed very marked atrophy in three others, the periods of observation varying from five to thirty-two months. In one case, the ovary remained apparently the same size at the end of seventeen months, and in the ninth both ovaries had been implanted, and both increased in size. In this instance, it became necessary after a year and a half to extirpate the ovaries, as they had become extremely painful, and a condition of excessive menorrhagia and metrorrhagia had developed. After removal of the ovaries, these symptoms entirely disappeared, and the patient regained good health. Microscopic examination showed some fibrous and hyaline changes in the stroma, numerous developing and

cystic follicles, and a well-developed but degenerating corpus luteum. The tissue appeared incontestably to have been living and functioning, but showed distinctly beginning degenerative changes. *Functional Results:* In five cases the implanted ovaries became at times (usually, but not always, immediately preceding menstruation) congested and painful; in the other four patients no such disturbances were complained of. In two instances, a hysterectomy was performed, and subsequent menstruation could not therefore be expected; in six of the remaining seven cases some evidence of menstruation became manifest, but in only one patient was a fairly normal menstrual life established. In all the others, menstruation was distinctly abnormal, being either irregular from the start, or regular for a short time, then becoming irregular, scanty, and finally ceasing, or in one instance, as already mentioned, giving place to excessive hemorrhages. To summarize; De Rouville was able to see a real permanent advantage to the patient from the graft in but one instance; in a second there was a definite benefit for a short time only, and in a third there was some questionable benefit. The others were not in the least improved, and in some cases harm was apparently done—at least disagreeable sequelae followed. De Rouville is therefore decidedly opposed to the use of grafts as a routine measure, and thinks that with our present technique the most that can be expected from them is the production of a gradual instead of an abrupt loss of the ovarian secretion.

Ovarian Secretion and Uterine Fibroids.—An attempt has been made by MAYER and SCHNEIDER (*Münch. med. Woch.*, 1914, li, 1042) to determine by means of the Abderhalden reaction whether there is any functional disturbance in the ovaries of patients suffering from uterine fibroids. While their investigations as reported are rather few in number, and by no means conclusive, they represent a somewhat new point of attack upon this much discussed subject, and present therefore some points of interest. The sera of thirty myoma patients were tested out by Abderhalden's dialysis method against extracts of their own ovaries (removed at operation), and against ovaries from other myoma patients, from carcinoma patients, pregnant women, and, so far as possible, women suffering with no genital disease. The ovaries from the carcinoma cases, and other extra-genital conditions, gave in every instance a negative reaction; in about 50 per cent. of the tests with ovaries from another myoma patient the reaction was positive, while in a considerable majority of those with the myoma patient's own ovaries a positive result was obtained. It has been shown by Abderhalden, as well as others, that the reaction is positive with a specific organ only when either the internal secretion of that organ is altered from the normal, or when anatomic changes are present in it amounting to practical destruction. Since we know from histological studies that the latter is not the case with regard to ovaries associated with uterine myomas, the causes for the positive reaction in so many instances must lie, Mayer and Schneider think, in a disturbance of the ovarian secretion, or, as they term it, a "dysfunction" of the ovaries. They believe that this is primary, and the development of the uterine tumors secondary, not *vice versa*. They believe also that the sterility, which so often accompanies uterine fibroids, is neither the result nor

a cause of the tumors, but that it likewise is a result of the disturbed ovarian function, as is the marked delay and irregularity in the onset of the menopause, which is often seen in these cases.

Dissection of the Ureter in the Radical Operation for Uterine Carcinoma.—MAYER (*Zeitschr. f. Geb. u. Gyn.*, 1914, lxxv, 399) says that while in many cases the ureter is easily found by the process of separating from above the layers of the broad ligament, in occasional instances this becomes very difficult, especially in the presence of senile or inflamed tissues. Moreover, at times numerous branching veins are present throughout the whole of the broad ligament, and give rise to exceedingly annoying hemorrhage as they are ruptured in separating the layers. In such cases, he has found the following slight modification of the usual technique of great service: The ureter can almost always be distinctly seen shining through its peritoneal covering in the higher portion of the posterior pelvic wall, or at the point where it crosses the great vessels. If the operator, after severing the round ligament and adnexa, draws the uterus forcibly forward and to the opposite side, before any dissection has been done to disturb the natural relations, it is always easy to trace the ureter down by sight to its point of entrance into the parametrium. If a small longitudinal incision be made in the peritoneum at this point, immediately over the ureter, the latter will be exposed without having separated any of the tissues of the broad ligament, and therefore without the production of any hemorrhage. If now the ureter is lifted by means of a long blunt hook, or similar instrument, to one side or the other, the entire posterior layer of the broad ligament can be cut through low down, exposing the uterine artery and ureter in their entire course through the ligament, without the necessity for any blunt dissection of tissue. By this means, it is possible to remove a larger amount of parametrium than by the usual methods, and the uterine artery is easily exposed for ligation, without any danger to the ureter.

Action of Ovarian Lipoids upon the Genital System.—An interesting report has recently been made by ISCOVESCO (*Rev. de gyn. et de chir., abdom.*, 1914, xxii, 161) upon some experimental and clinical studies of certain lipoids obtained from human ovaries. As Iscovesco points out, every gland of internal secretion throws into the circulation a number of different lipoidal substances, one of which appears to have the specific action of stimulating the secretory activity of the gland itself. Fresh human ovary was found to contain about 3 per cent. by weight of total lipoids; extracting these by means of ether, acetone, chloroform, alcohol, etc., Iscovesco was able to distinguish five main groups, of which the fifth, or alcohol-soluble group is much the most important. By further solution and precipitation, this group can be subdivided into several different constituents, one of which, called by Iscovesco VDe, appears to exert a marked stimulant acting upon the ovary and whole genital system. It is a yellowish, wax-like substance; which for experimental and clinical use was made up in a 2 per cent. solution in oil. This solution may be injected hypodermically or intraperitoneally into laboratory animals, without any signs of irritation or infection. A series of young rabbits injected daily, or at inter-

vals of a few days, for a considerable period of time, all showed when killed and autopsied an enlargement of the ovaries and uterus to two or three times the size of these organs in controls; very young animals, in whom the injections were started at the sixth week and continued until the fifteenth week, showed by that time genital organs exceeding in size and weight those of adult animals. Practically no effect was produced in any of the experiments on any of the other organs, except the thyroid, which showed in the injected animals a slight increase in size; the effect here was much less, however, than in the genital tract. Iscovesco thinks the substance acts by direct stimulation of the genital centres in the central nervous system. For therapeutic purposes the same oily solution was given in 1 c.c. doses by deep injection into the gluteal muscles once daily, or four to six pills, each containing 2 cgm. of the lipoid, were given by mouth. The author reports astonishingly good results in the treatment of a number of cases of dysmenorrhea, amenorrhea due to ovarian hypofunction, and various nervous conditions in young girls, associated with irregular or painful menstruation, and probably having a basis in disturbed ovarian activity. Equally good results were obtained from the treatment of a number of patients suffering from the results of a natural or artificial menopause. Iscovesco does not think that the corpus luteum is responsible for the secretion of any substance essentially different from that elaborated by the entire ovary; if there is any difference, it is merely that the active substances are present in the corpus luteum in greater concentration. He has isolated from the corpus luteum a lipoid possessing identical chemical and physical characteristics with the one obtained from the ovary, and in a small number of animal experiments and therapeutic tests the results have been entirely similar.

DERMATOLOGY

UNDER THE CHARGE OF

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Disseminated Hematogenous Tuberculosis Verrucosa Cutis.—BOURGEOIS (*Dermatol. Zeitsch.*, Band xxi, Heft 1), who has made a most careful study of two cases of verrucose tuberculosis of the skin with multiple disseminated lesions, following, in the one instance measles, in the other scarlet fever, concludes that, besides the ordinary form which arises from local infection, there is a second, hematogenous in origin. The hematogenous form occurs chiefly in children with or without previous tuberculous symptoms, almost always after some one of the exanthemas, usually measles, much less frequently scarlet fever, and is not infrequently associated with other forms of cutaneous tuberculosis, such as the papulonecrotic tuberculide and lichen scrofulosorum. Clinically and histologically the hematogenous variety

agrees in every particular with that arising from local infection. While the lesions show a predilection for the extremities, the hands, feet, and elbows, they also occur on other parts, such as the nates, the trunk, the face, and genitalia.

The Significance of Cholesterin in Xanthoma.—SCHMIDT (*Dermatol. Zeitsch.*, Band xxi, Heft 2), employing the newer methods for the estimation of cholesterin in the blood and organs, has studied five cases of xanthoma, and found in all five patients a more or less considerable cholesterinemia, the cholesterin content being greatest in those in whom the clinical symptoms were most marked. The results of his investigation confirm completely the views of Pinkus and Pick that in patients with icterus and diabetes an infiltration of cholesterin fatty-acid esters takes place in the endothelial cells of the cutis and in the connective tissue, and that the deposition of these constitutes the chemical and histological characteristic of xanthoma. Schmidt believes that the cause of the xanthoma formation is to be sought in a constitutional anomaly in which an increase of cholesterin in the blood appears.

Dermatitis Papillaris Capillitii (Kaposi); Acne Keloid.—ADAMSON (*British Jour. Dermat.*, March, 1914), as the result of a recent study of four cases of this interesting affection, inclines to support the view of Kaposi that it is a chronic inflammation with the formation of new connective tissue which leads by pressure to atrophy of the glands and follicles. He regards friction by the edge of the collar as an etiological factor, and thinks a combined microbic and traumatic origin likely. He does not believe the acne bacillus nor the *Staphylococcus pyogenes* responsible for the affection, which in his opinion is not related to acne nor syccosis; nor is it true keloid. As to the treatment the author believes most success is obtained with the x-rays, using large and repeated doses.

Epidemic Alopecia Areata.—DAVIS (*British Jour. Dermat.*, June, 1914) reports an extensive epidemic of an affection resembling alopecia areata, occurring in an orphanage containing about 300 children, all of them girls. The first case was observed in March, 1913, and at the end of June there were no less than 174 cases. Daily washing with methylated spirit and soap and the application of ointments of β -naphthol and sulphur soon brought the diseases under control. A year later there was a new but less extensive outbreak which speedily yielded to treatment, which consisted this time in painting the patches with liniment of iodine. The patches were more like those of ringworm than ordinary alopecia areata, containing numerous stumps of hairs, but no fungus could be found. Although reporting the epidemic as alopecia areata, the author thinks it questionable whether the disease is properly so described.

Lichenoid Trichophytosis.—GUTH (*Archiv. f. Dermat. und Syph.*, Band cxviii, Heft 3), under the name lichenoid trichophytosis, reports fifteen cases of a disseminated or grouped lichenoid, occasionally psoriasiform eruption, which he has thus far observed only in deep

trichophytosis, especially in kerion of children. He regards the eruption as the expression of the trichophytin hypersensitiveness which appears in deep trichophytosis as an immunity phenomenon. By the application of trichophytin or the trichophyton to specifically hypersensitive skins analogous changes may be produced. The pathogenesis of the spontaneous exanthem is not yet explained.

Fungus Affections of the Hands and Feet.—KAUFMANN-WOLF (*Dermatol. Zeitsch.*, Band xxi, Heft 5), under the above title, reports twenty-five cases of eruptive disease situated on the hands and feet, resembling at times dysidrosis at others eczema, in which various fungi were demonstrable. In 17 of these cases the trichophyton was present; in the remainder various other fungi were found. The author concludes that fungous affections of the hands and feet appear frequently under the picture of dysidrosis or of eczema. The chief symptom is deep-seated, grouped vesicles, which are inclined to suppuration and seldom ooze. The vesicles always lie within the epidermis, and, notwithstanding the absence of recognizable fungous elements in their contents, are infectious, as is shown by culture. The fungus is found in the uppermost layers of the epidermis.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Diagnosis between Exudates and Transudates.—MAURICE VILLARET (*Jour. de Physiol. et de Path. générale*, May 15, xv, No. 3) publishes two articles dealing with the methods at his disposal for distinguishing exudates from transudates. In the beginning he deals with the various reactions with which we are already familiar. The Rivalta, dating from 1895, consists in the use of distilled water faintly acidulated with acetic acid into which is gently dropped one drop of the fluid to be tested. In the case of a positive reaction, such as is given by an exudate, the drop descends, slowly becoming turbid, and finally bluish-white. As to the explanation of the reaction, Villaret favors the view of Patcin, that the reaction is due to a specific albumin, acetoglobulin. It must be admitted that the subject has been widely debated without any fixity of opinion being as yet reached. The reaction of Gangi consists in taking from 3 to 4 c.c. of hydrochloric acid in a test-tube, and laying on top of it, carefully, 4 or 5 c.c. of the fluid to be tested and leaving it for some hours. If the reaction is positive, as occurs with an exudate, the upper fluid becomes turbid,

and there is a second ring of marked turbidity half way between the turbid disk lying next to the hydrochloric acid and the top of the fluid. Coagulation in the supernatant fluid is also an indication of positive result. The collargol test is made with a solution of collargol of the strength of 1 in 1000, freshly diluted to a strength of 1 in 25,000. Five test-tubes are filled two-thirds full of this solution, and into the first four are put 2, 5, 10, and 20 drops respectively, of the fluid to be examined. Mixed and carefully set aside away from the dust, they remain for twelve or fourteen hours before being examined. A negative result is shown by perfect limpidity of the solutions, and is to be expected in the presence of an exudate. Villaret considers that a positive reaction with the Rivalta and Gangi test with a negative collargol allows one definitely to conclude that one is dealing with an exudate; and on the other hand, a negative Rivalta and Gangi with a positive collargol test allows one to be certain that one is dealing with a transudate, and that these chemical tests suffice even in the absence of cellular examination, although the latter is highly desirable. In a second paper in which he deals with the examination of the cells in conjunction with the previously mentioned tests, Villaret divides ascitic fluid into three types. Of these the first is ascitic fluid occurring from mechanical causes such as one finds in blocking of the inferior vena cava, and in portal congestion. Endothelial cells are entirely or largely predominant, and the Rivalta and Gangi reactions are negative, and the collargol positive. The second division, ascites from inflammatory causes, may be characterized by lymphocytosis, as in tuberculous peritonitis, or by a mixed cellular picture where the endothelial cells demonstrate that portal hypotension is playing a part, as it might be expected to do in syphilis or cancer of the liver; or yet again by predominance of polynuclears, indicating that the ascites is infected to some degree. With such fluid the Rivalta and Gangi are positive, while the collargol reaction may be either positive or negative. From the two foregoing classes one may be able to distinguish mechanical ascites with secondary infection, in that the cellular picture becomes modified little by little, the polynuclears and lymphocytes progressively replacing endothelial cells. This change is preceded generally by a transformation of the Rivalta and Gangi test which from being negative, become positive: that is, from indicating a transudate, come to suggest an exudate. Finally, in far advanced cases, the transudate origin of the fluid can sometimes be determined by the persistence of the collargol positive reaction, which in the course of time becomes negative, showing that the infection has died out, or has at least been superseded by a mechanical transudate.

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ORIGINAL ARTICLES

**SEVERE ANEMIA CONNECTED WITH GASTRO-INTESTINAL
DISEASES.¹**

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ALTHOUGH not aware of the frequency of pernicious anemia in the United States, I believe that in Europe it is becoming more and more frequent. When studying the different kinds and manifestations of intestinal dyspepsia, I met with more or less severe anemia, and will state the relationship existing between these two morbid conditions.

Combe, Addison, and Biermer first described certain cases of anemia, marked by their intensity and fatal issue, as idiopathic or pernicious anemia. They based their reasons for separating this particular anemia from the common type not only on the serious character of its clinical symptoms—high degree of blood changes, fever, extravasations of blood, digestive troubles, etc.—but also on the absence of any organic lesion which could be regarded as the origin of the disease and the lack of any conceivable etiology. This manner of defining a new clinical disease chiefly by negative symptoms, though corresponding to the state of science at that time, could not be satisfactory. Thus the discussion about the nature and the conception of the disease began and has continued, producing numerous facts and theories, but not at all solving the problem.

¹ Delivered before the Harvey Society, October 18, 1913.

One of these facts is the discovery, made by Russian and Danish authors, especially by Rosenquist, Schaumann, and Talquist, that infection with *bothriocephalus* is able to cause a form of progressive anemia which by no means can be separated from Biemer's pernicious type. With that the idiopathic or primary character of the disease became doubtful. But though there were found subsequently other causes of the disease, as syphilis (Fr. Müller), pregnancy (Gusserow), etc., the remaining number of unexplained cases was still large.

In interpreting these cases from 1900 to the present time, two different theories are mostly discussed: according to one of them, inaugurated by Paul Ehrlich, the characteristic sign of the disease is the megaloblastic degeneration of the blood-forming structures; the other, advocated by W. Hunter, starts from the hemolytic nature of the disease and supposes its origin to be found in a more or less specific affection of the gastro-intestinal tube.

Ehrlich's hematological studies, by means of differential staining, led him to the conclusion that a distinct type of bone-marrow change, which causes the appearance of large and intensely colored, partially nucleated red corpuscles—megalocytes and megaloblasts—cell forms which under normal conditions appear only in embryonic life, is not only the essential symptom but even the cause of pernicious anemia. He and his followers (Lazarus, Engel, Naegeli, and other hematologists) speak of pernicious anemia only if this sign and some other blood changes, as increased color-index, poikilocytosis, diminished number of leukocytes, with comparative increase of lymphocytes, are evident.

There can be no doubt that by accepting Ehrlich's theory the conception of the disease, given by Addison and Biemer, is changed to some extent, for clinical observation shows that megaloblastic degeneration may be present in some cases of common (secondary) anemia and absent in others belonging to the idiopathic group. The megaloblastic type of blood formation, though a characteristic symptom of the disease, as is the pigmentation of internal organs and the tendency to hemorrhages does in no way explain the etiology. If pigmentation is the cause of hemolysis, the changes in blood formation must be taken as reactions of the bone marrow to the unknown cause of hemolysis (Naegeli).

Hunter was the first to perceive the hemolytic nature of pernicious anemia. After him this form is distinguished from all other forms by the excessive presence of iron in the liver, due to the more or less continuous destruction of red corpuscles within the portal circulation. Though he could not prove the presence of the hemolytic process itself nor produce the hemolytic substance from the organs, he tried to confirm his theory by indirect arguments, especially by demonstrating the constant presence of glossitic lesions, which he supposed to be caused by streptococci

infection, and by finding an increased amount of aromatic sulphates and other products of intestinal putrefaction in the urine of his patients.

Hunter's observations, at first neglected in consequence of the attention generally bestowed upon Ehrlich's studies, have found valuable support through E. Grawitz and other clinicians. But his theory could not be accepted before the supposed hemolytic principle was brought into evidence. This was done in 1907 by Tallquist in bothriocephalus anemia, the best studied form of enterogenous anemia. Only a small percentage of patients harboring tape-worm suffer from anemia. Tallquist estimates the occurrence to be less than 1 per cent. Though this disease in its severer forms shows all symptoms of pernicious anemia, the blood is by no means always megalocytic or even megaloblastic. Sometimes in the beginning there are found glossitic lesions analogous to those described by Hunter. Nitrogen metabolism is periodically altered so that increased decomposition of albuminates must be accepted (Rosenquist). The substance which causes hemolysis is produced in the tape-worm itself, not in the healthy one, but in degenerated parts of it by an autolytic process. It is a cholesterin ester of oleic acid, which in small quantity also may be obtained from different normal organs. If the bothriocephalus is removed by efficient treatment the patients may entirely recover, but in some cases there still remains an increased tendency to the recurrence of anemia (Schaumann).

Bothriocephalus is not the only worm the presence of which gives rise to anemia, as the hook-worm, which sucks blood from the mucous membrane, thus leads to successive anemia. But as it produces no toxin, the megaloblastic blood degeneration is missing. On the other hand, there have been described some undoubted observations of the pernicious form connected with the common tape-worm (*Tenia saginata*) and with trichocephalus, round-worm, and certain protozoic infections. Even in tropical sprue an anemic condition of severe character is sometimes seen, although exact investigations of blood changes are not yet published.

Regarding the hemolytic nature of bothriocephalus anemia, it is natural to suppose similar conditions in other forms of anemia connected with gastro-intestinal disorders. Besides the large class of unexplained idiopathic anemias, there are two more morbid states which from this point of view excite our interest—namely, the coincidence of a small non-ulcerated stomach cancer, with progressive anemia of the megaloblastic type, and the development of the same pernicious form in the course of cicatricial stenosis of the small intestine.

As regards the first condition, the fact is well known that the so-called cancer anemia appears especially in cancers of the gastro-intestinal tract. Though the blood generally does not show the

characteristic signs of toxic bone-marrow reaction, hemolytic substances comparable to those of the bothriocephalus body have been separated from cancerous tissue by Kullmann, Tallquist, and others. They may be, but seldom are strong enough to overcome the regenerative power of the blood-forming organs. In the cases referred to, the postmortem examination did not exhibit any other cause of the anemia, as, for instance, inflammation of the mucous membrane, cancerous degeneration of the bone marrow, etc. v. Noorden, Israel, Scott, Bloch, Lazarus, Nauer have observed such cases, and I can add two of my own. Shall we regard this coincidence as chance? Are there two different diseases coexistent? I think it is difficult to deny entirely any connection between them.

The second condition, cicatrised tuberculous stenosis of the small intestine, accompanied with pernicious anemia, was first described by Faber and Borchgrevink. Most of the cases hitherto known showed no fresh ulcerations nor any notable inflammation. In my own two observations even microscopic investigation demonstrated only the same state of insignificant lymphocytic infiltration of the mucous membrane, as in other cases of pernicious anemia. Neither the preëxisting tuberculous ulceration nor the scars, but only the irrigation of the intestinal walls following the chronic retention of the contents, can be regarded as the etiology.

The group of unexplained cases of pernicious anemia in relation to gastro-intestinal troubles now claims our attention. Biemer has described certain digestive disturbances, as anorexia, gastric discomfort, weak digestion, and periodic diarrhea, as the chief symptoms of the disease called after him; but he regarded them as consequences of the anemia, as did succeeding observers except Hunter. Hunter says: "A history of antecedent gastric or intestinal disturbances was found in each of twenty-five cases. In no case were these of sufficient character or intensity to account for the supervention of such an intense degree of anemia. The various disturbances connected with this tract have an important significance, not as a cause of the disease, but as symptoms of the gastric and intestinal infective lesions associated with the disease." In other words, anatomical lesions, especially the infective glossitic changes, are the chief factors; the digestive troubles are only the mild manifestations of these lesions.

According to the more physiological point of view of modern clinical investigation we will first consider these functional disorders. The fact of the constant absence of hydrochloric acid in the gastric contents of all patients suffering from pernicious anemia was somewhat neglected until Martius found out that we had to deal not only with a defect of hydrochloric acid, but of the whole gastric digestion, *i. e.*, with achylia gastrica. Even this fact did not attract much attention, for by the more common use of the stomach-tube it soon became evident that many persons who

have no gastric juice do not suffer from any digestive trouble, and that this condition does not depend necessarily on atrophy of the gastric glands. But the conception has considerably changed. Since Oppler and Einhorn first described chronic diarrheas following gastric achylia the different forms of gastrogenous intestinal dyspepsia have become an object of clinical interest, the consequences of which cannot yet be fully estimated. Faber, who analyzed 207 cases of achylia, found in 22, or 11 per cent., marked signs of pernicious anemia, and in 22 others a hemoglobin of less than 50 per cent. While the anemia in these latter cases only showed the character of a serious chlorosis, in the others all the blood changes of the pernicious form were present; increased color-index, poikilocytosis, leukopenia, and megaloblastic degeneration of the red corpuscles. Furthermore, Faber observed a number of patients suffering from severe anemia, whose achylia had already existed and had been proved many years before they fell sick with anemia. This fact led him to the conclusion that pernicious anemia is not, as generally supposed, the cause of gastric achylia, but, on the contrary, the result of it.

Coming now to the intestines, it was Grawitz who, following Hunter's suggestion, attached most weight to enterotoxic products, which he supposed to result from insufficient or faulty denaturation of the albuminates. Unfortunately, he also was unable to produce any argument which could confirm his theory. I therefore first undertook to study the frequency and kind of the intestinal troubles, mentioned by most authors as a symptom of the disease, but not yet analyzed by anyone.

Among my patients suffering from idiopathic pernicious anemia there were sixteen, the third part of all observed, who showed more or less marked signs of intestinal disorders. They mostly had periodic diarrhea, or diarrhea alternating with constipation. Generally the diarrhea was of an insignificant degree, and was not accompanied with colicky pains.

When examined by means of my test-diet or similar food, the feces were of a pulpy consistency, and had an offensive odor, which sometimes was distinctly sour. Corresponding to that the reaction was either markedly alkaline or acid, the normal test-diet stool being nearly neutral. When ground up with water to a fluid consistence, often small flakes of mucus could be seen, whereas larger particles were constantly missing. A few times the whole mass showed a mucous condition, though no flakes could be isolated. Chemical tests showed that this condition was caused by the presence of a large quantity of nucleoproteid, a product of the intestinal epithelium, which under normal conditions appears only in small quantity.

As to the remains of food, connective tissue was often found, due to the lack of gastric juice. Macroscopic remains of muscular

tissue seldom could be seen, but often increased quantities of microscopic muscle fragments. Starch granules colored blue with iodine and numerous needles of fatty acid and soaps were easily defined by the microscope. The fermentation test at times was positive.

Interpreting these facts we have to deal with a kind of intestinal dyspepsia, sometimes associated with an irritation of the surface epithelium and periodically bringing about a transitory inflammation of the mucous membrane. These are the same conditions as found in other non-anemic cases of gastric achylia; they offer the real features of what are called gastrogenous dyspepsia. As in all these forms their appearance changes, now present for a shorter or a longer time, now ceasing suddenly and permitting stools of completely normal character or a state of mild constipation. Therefore it may happen they are only identified by carefully inquiring into the previous history, as they are absent during the period of observation. In the majority of my cases transitory diarrhea and gastric achylia, which was present in all my cases except one, preceded the development of the anemia many years.

There is marked harmony between my observations and those of Faber, especially as to the pre-anemic digestive troubles. Endeavoring to answer the question in which way achylia may lead to anemia, Faber believed it to be by way of the intestine. According to his suggestion the lack of hydrochloric acid gives rise to the establishment of hemolytic bacteria in the small intestine, but he did not prove either the existence or the nature of the supposed intestinal disorders. This was omitted by all the earlier authors, as, for instance, Martius, who sought the cause of pernicious anemia in atrophy of the mucous membrane, proceeding from the stomach to the duodenum and small intestine. As to my experience, not only is the frequency of intestinal dyspepsia in pernicious anemia striking, but even more so in the frequent occurrence of various degrees of anemia in all forms of chronic intestinal dyspepsia. The percentage of serious forms of anemia occurring in the course of gastrogenous dyspepsia is much higher than that occurring in simple achylia not connected with diarrhea. Thus the common non-specific intestinal dyspepsia forms the missing link between achylia and pernicious anemia.

We cannot here thoroughly discuss the theories concerning the real causes of intestinal disorders following gastric achylia. Faber's suggestion, based on the passage of pathogenic bacteria through a stomach not containing hydrochloric acid, a theory established long ago by Baumann and his pupils, is indeed useful, because the condition of chronic intestinal dyspepsia cannot be understood without the coöperation of bacterial fermentation. But surely the lack of hydrochloric acid cannot by itself entirely explain the problem. The connective tissue and other food remains which

are not dissolved in the achylic stomach contents may be accused with more probability, as they are not only a lurking place, but also a good culture medium for decomposing bacteria, which under these conditions settle in the duodenum. Together with burdening of the intestine with insufficiently dissolved food, they slowly lead to a state of exhausted pancreatic digestion, which can sometimes be proved by the appearance of unchanged nuclei in the feces.

Turning now to the anatomical lesions, the glossitic changes known as Hunter's tongue can be observed in the majority of cases. Microscopic investigation shows proliferation of the epithelial covering alternating with atrophic spots, fissures, mild degrees of lymphocytic exudation, and other signs of chronic inflammation. Streptococcic invasion, found by Hunter, can only be regarded as accidental. It may also be noticed that irritability of the tongue, corresponding to the characteristic appearance, sometimes precedes the anemia (Matthes).

Faber and Bloch, who studied the microscopic structure of the stomach in achylia, found the lymphatic follicles enlarged and indistinctly shaped, lymphocytes more or less spread through the mucous membrane, and the glands diminished in number and size, doubtless signs of chronic inflammation, but no atrophy.

As to the intestine, the question introduced by Nothnagel as to whether an atrophic state of larger parts of the mucous membrane, like those occasionally seen in the stomach, are in any way to be found, can be answered in the negative. Though the macroscopic features of a thin, pale, and transparent intestinal wall, especially met with in cases of pernicious anemia, seems to disprove that careful microscopic examination of the whole intestine, prepared immediately after death, shows only the same pathological changes as in the stomach. Even by comparing the weight of the whole mucous membrane with that of a normal one, and by counting the number of Lieberkühn's glands in sections from different parts, Meyer and v. Lippmann in my laboratory, agreeing with Faber and Bloch, found no atrophy. There were the same signs of a slight chronic inflammation of the mucous membrane as found in the stomach. Only once did I observe a fresh inflammation in the lower part of the ileum.

Gathering up these facts, we must conclude that the anatomical lesions corresponding to the functional disorders do not show any specific character, that they must be regarded rather as the result than as the cause of the digestive disturbances. Hunter's suggestion of a primary infectious origin of pernicious anemia is proved neither by anatomical nor by bacteriological facts.

But the fact of coincidence of the gastro-intestinal lesions with the anemic condition cannot prove their causal connection. Are there any arguments to make evident the hemolytic nature of

these lesions? Though it is well known, and can easily be demonstrated, that the blood taken from the peripheral veins in pernicious anemia does not show or seldom shows signs of hemolysis, such as colored serum or decreased resistance of the red corpuscles to salt-solution, there are some remarkable facts supporting the theory of a hemolytic agent especially circulating in the portal venous system. The first, produced by Hunter himself, is the excessive accumulation of iron in the liver, which is more than three times as great as under normal conditions, and does not bear a correct relation to the amount of iron in the spleen and the kidneys. The other fact, exhibited by M. B. Schmidt and communicated by Matthes, is the reddish (hemolytic) color presented only by the portal lymph vessels and lymph nodes in patients who died from pernicious anemia.

Accepting the suggestion of a hemolytic agent entering into the portal system, the question arises whether it is produced in the chyme or in the mucous membrane of the bowels. The presence of an increased amount of hemolytic substances in the intestinal contents or in the feces, if ever proved—as it has not been—cannot satisfy us, because the decomposition of almost all sorts of food sets free transitory traces of oleic acid. This acid is shown by Tallquist and Faust to be an efficient hemolytic substance; the normal epithelium must be able either to withstand such a noxious substance or, if absorbed, to destroy its toxic character by changing its structure. By the same reason the researches of Lüdke and Fejes, who extracted hemolytic substances out of the different intestinal bacteria, especially from the *Bacillus coli*, isolated from pernicious anemia, do not explain anything, as so far there is no evidence that the bacteria penetrate the covering epithelium and grow within the mucous membrane.

On the other hand, Korschun and Morgenroth produced hemolytic lipoids from different normal organs; for instance, from the mucous membrane of the intestine, the pancreas, etc. Starting from that fact, Berger and Tsuchiya in two of our cases of pernicious anemia immediately after death prepared the mucous membrane of the whole gastro-intestinal tube. The lipoids extracted from the stomach, and even more from the small intestine, showed a hemolytic power about ten times higher than those of normal organs. I believe this result to be of great importance, although Ewald and Friedländer could not confirm it. But they omitted to examine fresh organs.

Remembering the microscopic signs of chronic inflammation, mentioned before, we are justified in supposing certain degenerative changes in the mucous membrane of the small intestine which may set free hemolytic substances. It is obvious that the constant absorption of even a small quantity by an organ, especially des-

tined for absorption, can exhaust the reproductive power of the bone marrow.

Another fact, just stated by Kabanow in my laboratory, may confirm this suggestion. Working with the new Abderhalden method of proving the origin of diseases by searching for the so-called specific protective ferments circulating in the blood, Kabanow in three cases of pernicious anemia found the mucous membrane of the small intestine regularly, that of the stomach only once, but that of the colon, liver, etc., never decomposed by the serum. This means that the small intestine and in a lesser degree also the stomach, undergoes degeneration.

If the experiences hitherto spoken of seem to confirm the causal connection between certain digestive disturbances and the development of pernicious anemia, I do not believe that all cases of this disease have this origin. Only one-third of the patients suffering from pernicious anemia show marked intestinal troubles, and the number of dyspeptic persons who acquire severe anemia is not higher. Moreover, experience shows that the anemic condition when once developed, does not always go parallel with the intestinal troubles. While the latter improve and relapse, the anemia often maintains its progressive character even when the digestion has improved under careful treatment. Schaumann studied the fate of his patients who recovered from bothrioccephalus anemia and found that part of them still inclined to relapsing anemia. This observation and other circumstances induced him to believe that a constitutional state forms the basis upon which different lesions may give rise to pernicious anemia. Indeed, Bartlett, Pateck, Matthes, and others, saw striking examples of family or hereditary development of the disease. Pernicious anemia can be produced also by causes which have no connection with the gastro-intestinal tube, such as lues, pregnancy, septic infection, chronic nephritis, etc., though the intestine as the chief place of absorption prevails. If the experiment newly made by Eppinger and Delcastello, that extirpation of the spleen is able to cure certain cases of pernicious anemia, should be confirmed in the future, we must deal with the possibility of an accumulation of the hemolytic agent in the spleen, as Banti supposes to take place in the disease called after him.

The blood changes of pernicious anemia, interpreted by the hematologists as a degeneration of blood formation, leads to the same suggestion of a various etiology of the disease. There is no proof that only toxic irritation of the bone marrow produces the megaloblastic type of blood formation. Every sort of exhaustion can do the same. Often the first attack can be combated by stimulating the blood-forming organs with arsenic. If the cause of permanent blood dissolution is at once removed the anemia may disappear.

It is useless to discuss a problem which cannot be solved with

our present knowledge. Turning to the more practical question, Do the facts in any way influence our treatment of pernicious anemia? Grawitz, who first accepted Hunter's theory, based his opinion more on his successes in treating the anemic with a carefully composed diet and with systematic washing of the stomach and colon than on pathological investigations. We all know the difficulties of feeding these patients. The irritability of the tongue and stomach is extreme, and makes them refuse all except soft food. Regarding the constant lack of hydrochloric acid in the stomach and the intestinal dyspepsia depending on it, we can give some rules which must be observed in the diet. The first is to banish all irritating substances, such as salt, spices, too hot or too cold food, sparkling drinks, high percentage alcoholics, etc. All food must be minutely chopped or mashed because the stomach, which by its juice should assimilate the injected material, does not functionate as it should. By the same reason all raw food, as fruits, salads, raw or smoked meat, etc., are not permitted. Whatever is eaten must be thoroughly cooked or grilled.

As to the combination of the food, I do not agree with Grawitz, who, fearing that the decomposition of albuminous material could supply the hemolytic agent, put his patients on a vegetarian regime. Personally, I do not prefer any particular food, but adapt the diet in each case to the report of the feces examination, which must be repeated at least every other day. If the stool shows fermentation of carbohydrates (acid reaction, remains of starch and iodophilous bacteria, production of gas in the thermostat), all vegetables, potatoes, rice, bread, sometimes even sweets, must be avoided for some days. Later, under control of the feces they may be allowed. On the other hand, evident putrefaction of the stool (with alkaline reaction, increased fragments of muscle fibers, etc.) affords restriction of the albuminous food (meat, eggs, etc.), and a more farinaceous or milk diet. Changing the regime has of itself a good effect.

As achylia of the stomach is a constant symptom of pernicious anemia, it is usual to give the patients hydrochloric acid with the meals. I sometimes exclude arsenic and other drugs, but am convinced that by regular use of hydrochloric acid not only the intestinal disorders will be diminished, but also the anemic state can be considerably improved. Grawitz, Cottan, and others have reported cases treated and cured by hydrochloric acid alone. If hydrochloric acid proves useless, I recommend systematic washing of the stomach with physiological salt solution or salicylic acid solution (1 to 1000). More efficient are insufflations of oxygen directly into the intestine by the duodenal tube. Grawitz applied lavage of the colon with 2 per cent. salt solution, and emphasized their effect. My own experience is too slight to form an opinion about them, but I believe it is better to wash the duodenum than

the colon. I prefer these methods to the use of disinfecting drugs as none of them has proved satisfactory.

As mentioned previously, the improvement of anemia does not always keep pace with the disappearance of the intestinal disorders, yet subsequent care for the latter has a real effect also on the former. Preceding the development of anemia, the digestive troubles should be noticed as early as possible and submitted to careful treatment. Prophylaxis is always safer than healing the fully developed disease. Here, as in other branches of internal medicine, our motto must be: *Principis obsta*.

THE RELATION OF GLYCOSURIA TO PITUITARY DISEASE AND THE REPORT OF A CASE, WITH STATISTICS.*

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THE extraordinary influence of the pituitary gland upon the metabolism and development of the body is now universally conceded. Cushing¹ has grouped the disturbances of the hypophysis cerebri under the term "dyspituitarism," the manifestations being due partly to primary involvement of the gland and partly to the effects of pressure upon neighboring structures.² That pituitary disease, however, occasions secondary alterations in the functions of certain internal secretions is quite probable. In support of the fact that hyperthyroidism may be consequential to lesions of the hypophysis, we desire to report a case of acromegaly with glycosuria in which there were manifestations of exophthalmic goitre.

The patient, A. H., aged forty-six years, occupation cook, weight 170 pounds, and height 5 feet 9½ inches, first fell under the care of my surgical colleague, Dr. William L. Rodman, in the Medico-Chirurgical Hospital, at which time she was suffering from a gangrenous wound, inflicted by a fish bone, of the left hand. On December 12, 1913 (a few days later), the patient was referred to the medical service—to us—for study and treatment. It should be stated at the outset that the left hand continued to show swelling, was very painful, and presented a large gangrenous ulcer on the

* Read before the Association of American Physicians, at Atlantic City, May 13, 1914.

palmar surface of the index and middle fingers, with slow extension until death occurred. Polydipsia, polyuria, and glycosuria, as well as bulimia, were all prominent features throughout the illness. The percentage of sugar at first was 5 per cent., but at the end of one week it rose gradually to 7 per cent., and remained at this level until the end.

The typical symptoms of acromegaly were in evidence, as the accompanying photographs would also indicate. The hypertrophy involved both the bones, especially of the face, hands, and feet, and the soft parts, the lips being much thickened. According to the history the bones of the hands and face began to enlarge four years ago, while the glycosuria set in about two years later. An x-ray examination by Dr. George E. Pfahler showed marked lipping at the edges of the articular surfaces of the metacarpal bones and phalanges, such as is found in acromegaly, and also a tumor of the pituitary gland, with absorption of the clinoid processes.

The diagnosis of associated hyperthyroidism was quite apparent from the noticeable enlargement of the thyroid gland, together with tremor, tachycardia, and exophthalmos. The goitre was bilateral, although asymmetrical, soft, and elastic, but gave no suggestion of fluctuation. On auscultation a systolic arterial murmur was heard over the larger right lobe of the thyroid gland. The exophthalmos, although moderate in degree, was, as is the rule, an obtrusive symptom. The indications of exophthalmic goitre were most probably developed after the glycosuria had existed for an indefinite period of time, although being, as is usual, of insidious origin, it was impossible to fix the precise date of onset.

The Wassermann reaction gave a negative result. Two weeks prior to the fatal termination, bed-sores developed, and despite our best efforts to arrest them, became extensive and contributed to the gradually increasing exhaustion until the end was reached. During the twenty-four hours preceding death, coma, from which it was impossible to arouse the patient, developed. Death occurred on January 16, 1914. No autopsy was permitted.

Marinesco³ reports a case showing, similarly, the association of acromegaly, diabetes mellitus, and certain unmistakable indications of Basedow's syndrome. Etiological significance in the production of hyperthyroidism has been attributed to acromegaly, but the nature of the relationship is not perfectly understood. Dock states that the diabetes arising in the course of acromegaly is cerebral and due to the pituitary disease, as shown by the fact that "diabetes is most marked with the largest tumors,"⁴ an observation confirmed by our studies. According to Borchardt⁵ this dictum is also corroborated by experiments on animals.

The metabolic changes caused by acromegaly are inconstant. Borchardt⁶ in reports of 176 cases found diabetes recorded in 63 or 35.8 per cent., and alimentary glycosuria in 8 more. J. H. W.

Rhein⁷ studied in the literature the symptomatology of 169 cases of tumor of the hypophysis and found glycosuria in only 7, or 4.1 per cent. Among these, 52 instances of acromegaly, or 30.8 per cent., occurred.

The purpose of the present statistical investigations has been to collect all of the cases of pituitary disease recorded in literature since the publication of the paper by Borehardt, or, in other words, a period of five years terminating December 31, 1913; also to either confirm or refute certain views which have been advanced in the past, notably that by Kollaritz,⁸ that glycosuria does not



FIG. 1.—Showing hypertrophy of bones of face, characteristic of acromegaly.



FIG. 2.—Hypertrophy of bones of hand typical of acromegaly.

occur in tumors of the hypophysis without associated acromegaly. Again, it was hoped that the facts and data thus gleaned might aid in clearing up the question of the relation of hypo- and hyperthyroidism to acromegaly on the one hand and glycosuria on the other.

Our collective investigations yielded a total of 246 cases of hypophysial disease. In 183 cases the urinary findings were mentioned and showed 28 instances of glycosuria, in 9 of which the condition was intermittent, and the subjoined table represents an analysis of these cases.

Author.	Age and sex.	Lesions of pituitary.	Acromegaly.	Glycosuria.	Other ductless glands.	Remarks.
Cushing ¹⁶	36 yrs. F.	?	Absent (hypopituitarism)	Glycosuria, intermittent Polyuria, constant	No mention	
Cushing ¹⁷	40 yrs. M.	Tubercle of pars-anterior	Absent	Glycosuria, intermittent Polyuria constant	No mention	Glycosuria developed one year after operation.
Kocher ¹⁸	30 yrs. F.	Sarcoma	Present	Diabetes, persistent	Thyroid, small Thymus, persistent	Patient operated upon.
Lucien and Parisot ¹⁹	65 yrs. F.	Tuberculosis	Absent	200 to 300 gms. in 24 hrs.	Pulmonary tuberculosis; pancreas normal.
Shoemaker ²⁰	35 yrs. F.	Adeno-carcinoma	No mention	Glycosuria shortly before death	Thyroids and adrenals, normal	Bitemporal hemianopsia.
Messedaglia ²¹	Present	Glycosuria preceded by hypophysial symptoms		
Church ²²	14 yrs. M.	Hemorrhagic cyst	Absent (infantilism)	Diabetes at 3½ yrs., duration not stated	No mention	Right temporal hemianopsia.
W. Romelaere ²³	...	Sarcoma	Present	Diabetes mellitus	Cirrhosis of pancreas and suprarenal glands	Blind. Death from bronchopneumonia.
Launois and Cleret ²⁴	33 yrs. F.	Sarcoma	Absent (hypopituitarism)	Diabetes mellitus	Bilateral hemianopsia, mental torpor.
Moskalew ²⁵	52 yrs. F.	Epithelioma	Absent	1 to 4.5 percent. sugar		
Foucault ²⁶	?	Tuberculosis	?	Diabetes mellitus	?	Thesis inaccessible.
Goldscheider ²⁷	51 yrs. F.	No tumor; assumes hypophysial alteration	Present	6 to 8 per cent. of sugar	Right ovary missing; thyroid and other ductless glands not mentioned	Glandular extracts had no effect. Exophthalmos present.
Marck ²⁸	26 yrs. F.	Present	Began eighth month of pregnancy, disappeared after delivery	No mention	Primipara developed acromegaly late in pregnancy.
Echevarria ²⁹	...	?	Present	Diabetes mellitus	Paper inaccessible.
Medigreceanu and Kristeller ³⁰	28 yrs. M.		Present	100 to 150 gms. per day; later increased tolerance		
Goetsch, Cushing and Jacobson ³¹	Present	Glycosuria, later increased tolerance		
Bittori ³²	38 yrs. M.	Tumor (gumma?)	Present	Alimentary glycosuria	Thyroid normal	Binasal hemianopsia, Wassermann positive.
Amsler ³³	41 yrs. M.	Tumor	Present	Diabetes mellitus during acromegaly	Hyperplasia of spleen, pancreas and adrenals	Arteriosclerosis present.
Cushing ³⁴	32 yrs. M.	Gumma of pars-anterior and intermediate	Absent	Glycosuria disappeared; polyuria persisted	No mention	Slight exophthalmos.
Fisher ³⁵	29 yrs. M.	Fracture at base of skull	Absent	Glycosuria, intermittent first, 24 hrs. after fall	No mention	Glycosuria attributed to irritation of posterior lobe by extravasated blood.
Hill ³⁶	18 yrs. M.	Cyst	Absent (Frohlich's syndrome)	Marked polyuria. Glycosuria cleared after operation	Thyroid and thymus not palpable	Operation caused marked improvement. Attributed glycosuria to intracranial pressure.

Author.	Age and sex.	Lesions of pituitary.	Acromegaly.	Glycosuria.	Other ductless glands.	Remarks.
Carnot, Rathery and Dumont ³⁷	58 yrs. F.	Hypertrophy	Present	80 to 295 gms. in 24 hrs.	Thyroid sclerotic and cystic; suprarenals and pancreas sclerotic and hemorrhagic; ovaries sclerotic	
Fink ³⁸	...	?	Present	Diabetes mellitus	?	Dissertation inaccessible.
Sainton and Rol ³⁹	16 yrs. F.	Tumor probably malignant	Absent	Diabetes of grave juvenile type	Thyroid atrophied and sclerotic	Bilateral hemianopsia; knee-jerks exaggerated; speech slow.
Genella ⁴⁰	45 yrs. M.	Probable tumor	Present (atypical)	Glucose, 3 to 5 per cent.	Difficulty in speech; reflexes diminished.
Meyer ⁴¹	Present	Diabetes mellitus	Associated with paranoia.
Grinker ⁴²	49 yrs. M.	Adenoma	Present	Intermittent and slight	Thyroid not palpable	Subject to epileptic attacks.
Anders and Jameson	46 yrs. F.	Tumor	Present	Persistently present, 5 to 7 per cent.	Well-marked evidence of hyperthyroidism	Gangrene of hand. No hemianopsia.

It will be observed from a glance at the above table that 16 of the 28 cases of pituitary glycosuria, or 57.1 per cent., showed acromegaly, while 10, or 35.7 per cent. failed to show the latter condition in association. In 2 cases the presence of acromegaly was in doubt, hence excluded. It is interesting to note that of the 183 cases of pituitary disease in which the urinary findings were given, 88, or 42.6 per cent. showed acromegaly, and of the latter only 16, or 18.2 per cent. showed the presence of sugar. Moreover, it is a matter of no less interest that in 91 cases of pituitary disease in which acromegaly was absent, 10 showed spontaneous glycosuria, and no mention was made of either hypo- or hyperthyroidism in these cases.

The foregoing facts are not in accord with the observations of Kollaritz,⁹ who recorded 52 cases of tumor of the hypophysis without acromegaly, of which not one was complicated by diabetes. Borchardt, writing in 1908, also affirms that since 1886 not one case of tumor without acromegaly was found in which glycosuria was associated. Sainton and Rol¹⁰ state that although pituitary glycosuria without acromegaly may occur, it is rare. Here it is to be recollected that when spontaneous glycosuria is absent from this tripod of conditions, experimental observation may show the presence of an alimentary glycosuria. For example, Borchardt¹¹ reports 10 cases of acromegaly without spontaneous glycosuria, of which 8 showed the alimentary form, applying the usual test. He claims that glycosuria in one of its forms is more regularly present in acromegaly than in any other disease.

As an examination of the above table with reference to the character of the hypophyseal lesions will show, there was tumor in

72 cases (of which 3 were specified as sarcoma, 2 as cyst, 1 adenocarcinoma, 1 epithelioma, 1 adenoma, and 4 as "tumor"), tuberculosis in 3, gumma in 2, hypertrophy in 1, fracture at base of skull with extravasated blood in 1, and lesion not stated in 8. The ages in our series were given in 21 cases, out of the total of 28, and found to average thirty-seven and one-quarter years, the period of life intervening between twenty-five and sixty years furnishing all save 3 cases.

In view of the fact that glycosuria not uncommonly complicates exophthalmic goitre, the question naturally arises whether in a case such as reported above it is to be attributed to the associated hyperthyroidism or to the hypophysial disease. As the result of the present investigations into the literature of the subject covering five years which ended January 1, 1914, there was but 1 case of hyperthyroidism in combination with pituitary lesions and glycosuria, out of a total of 28 cases recorded, namely, our own case herein reported, so that the role played by the thyroid gland in the causation of glycosuria in these cases would appear to be both trivial and obscure.

Cushing¹² states that in none of his 26 cases were there any symptomatic evidences of hyperthyroidism, but he found some degree of exophthalmos, which in all probability was a neighborhood effect of the tumor, to be common. On the other hand, Exner¹³ refers to two of Hochenegg's patients with acromegaly and partial glandular extirpation, in which subsequent enlargement of the thyroid, occurred. It is highly probable that the results of various observers will not be in agreement on the point at issue for the reason that some of the cases are studied in the stage of insufficiency while others are investigated in that of hyperthyroidism. The balance of evidence—experimental, pathological, clinical—is in favor of the view that insufficiency of the thyroid gland increases carbohydrate tolerance. A. Lorand¹⁴ believes that thyroidism is the dominating cause of the glycosuria in the rare cases in which pituitary disease and glycosuria coexist with Graves' disease.

Furnival found only 5 thyroids which could be considered normal out of 24 cases of acromegaly. Conversely, Schoneman's¹⁵ studies of the pituitary body in 85 cases of goitre revealed marked alterations in all but one instance. In this connection two facts pointed out by Cushing are worthy of note: (1) that the two glands have some histological points of resemblance, and (2) that both have a somewhat similar influence on skeletal growth. Microscopic changes in the thyroid in cases of acromegaly are for the most part a low epithelium with excess of colloid.

As pointed out by Cushing, care must be exercised not to confuse mere exophthalmos due to neighborhood pressure with associated exophthalmic goitre. For example, there were 2 cases of simple

exophthalmos, the result of mechanical pressure, and only 1 of associated Graves' disease in our series of 28 cases.

In concluding, there are two hypotheses pertaining to the combined conditions discussed above which have received considerable corroborative support from our statistical inquiries: (1) that the relationship existing between hyperthyroidism and pituitary glycosuria, with or without acromegaly, is a remote one, and (2) that pituitary glycosuria without acromegaly not uncommonly occurs (in 10 of our series, as against 16 in which acromegaly was also associated) contrary to the opinions of certain writers.

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THE VALUE OF TESTS FOR RENAL FUNCTION IN EARLY AND ADVANCED BRIGHT'S DISEASE.¹

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SINCE Richard Bright² described characteristic anatomical changes in various forms of kidney disease the problem of nephritis has occupied the attention of many observers. It is admitted that there are several types of nephritis, each one showing a different clinical course and different pathological lesions. It has been generally recognized that in the course of a nephritis, symptoms referable to toxemia have developed which have been given the inclusive name of "uremia," and that nephritic patients have died of uremia, of cardiac failure, or of some intercurrent cause. But it has been found impossible to predict in an individual case by clinical study alone what course the disease will take in its development or what anatomical changes will be found at autopsy. Therefore, during recent years, methods have been devised for estimating renal function in order to make possible an early diagnosis of existent kidney disease and to offer information in regard to its prognosis and treatment.

In 1881 Fleischer³ followed the excretion of nitrogen, sodium chloride, and phosphoric acid in a series of nephritic cases. His patients were given a known diet, and were controlled by normal individuals with similar food. Fleischer found that the excretion of nitrogen in ratio to its intake in the pathological cases showed considerable variation, that phosphoric acid was poorly excreted, while the chloride balance was nearly perfect. These observations justify the assumption that in a diseased kidney, different parts show selective excretory functions tending to retain certain substances from the diet and to excrete others normally.

In 1910 Schlayer⁴ and his co-workers began a series of experimental and clinical studies which have been of great value in the early diagnosis of abnormal renal function. Schlayer's original observations were based on acute experimental nephritis in rabbits. He injected potassium bichromate, cantharidin, or uranium nitrate into animals and produced a tubular, vascular, or mixed type of

¹ Read before the Section in Medicine of the New York Academy of Medicine, March 5, 1914.

² Guy's Hosp. Rep., 1836, i, 358.

³ Deutsch. Arch. f. klin. Med., 1881, xxiv, 129.

⁴ Schlayer and Takayasu, Deutsch. Arch. f. klin. Med., 1910, xeviii, 17; *Ibid.*, 1911, ci, 333; *Ibid.*, 1911, cii, 311; Verh. des. Cong. f. innere Med., 1912, xxix, 501; Beihefte zur med. Klin., 1912, ix, 211; Münch. med. Woch., 1913, ix, 800.

nephritis in which he studied renal function. He recognized the close relation which exists between renal blood-supply and the amount of urine excreted, and accordingly he studied general blood-pressure in his animals, changes in renal volume as recorded in an oncometer, and the diuretic response to various forms of stimuli, controlling the experiments by autopsy and histological examination. The various toxic substances produced different effects. In tubular nephritis Schlayer found that the renal vascular system reacted to vasodilators and constrictors normally. The urine, however, was dilute and the kidney was unable to concentrate and excrete sodium chloride when it was injected intravenously. In vascular nephritis, on the other hand, the kidney's concentrative powers were unaffected while the vascular response to vasomotor stimuli was lost or exaggerated. This led him to determine whether the excretion of other substances in addition to that of chloride might be used as a measure of the efficiency of the vascular or tubular apparatus of the kidney to replace observations with the oncometer. One of the prominent features of his experiments was the amount of fluid excreted. In tubular nephritis it was not remarkable; but in vascular nephritis it varied directly with the vascular functional condition. In cases where the renal vessels were hypersensitive to vasodilators there resulted a diuresis; when the vessels were insensitive there was oliguria. Thus the amount of urine obtained was one index to glomerular function. Voit⁵ discovered that if lactose was injected into an animal intravenously or subcutaneously the entire amount could be recovered in the urine. Schlayer, however, found in experimental nephritis that intravenous injections of this sugar were only well excreted when the renal vascular system was normal, and were held back when the glomeruli were damaged. Therefore he assumed that lactose in addition to water might be used as a test for the vascular condition of the kidney. Schlayer recognized the complexity of chloride metabolism. Duckworth⁶ had already introduced potassium iodide as a test for renal function, and Schlayer, comparing its excretion with that of sodium chloride, found that both were distinctly interfered with in tubular lesions. So Schlayer adopted the excretion of water and lactose as indicators of renal vascular activity, and that of sodium chloride and potassium iodide as measures of tubular activity. Experimentally there was a close agreement between the excretion of these substances and the respective types of nephritis, which confirmed Schlayer's views as to their place of excretion.

He turned these methods to the study of patients. His technique for the various tests was simple. While under observation

⁵ Deutsch. Arch. f. klin. Med., 1897, lviii, 545.

⁶ Saint Bartholomew's Hosp. Rep., 1867, iii, 216.

the patient was ordered a constant diet containing known amounts of fluid and salt. The total amount of fluid and sodium chloride excreted was followed from day to day. To make the lactose test 2 gm. of the sugar dissolved in 20 c.c. of distilled water were injected intravenously. After the injection the urine was collected at the end of four hours and every hour or two thereafter to twelve hours. Each specimen was tested for the presence of sugar with Nylander's reagent, and the total amount of sugar excreted was determined polarimetrically. Normally 60 per cent. or more of the amount injected was regained in from four to six hours.

On a certain day the patient was given 10 gm. of salt by mouth. Normally this should be excreted in from twenty-four to forty-eight hours, either by an increase of salt concentration in the urine or by diuresis. Schlayer found, however, that there were two types of abnormal salt excretion. In experimental tubular nephritis, with intact glomeruli, the kidney could not concentrate chloride and the salt was retained in the body. The specific gravity of the urine was low, and to this type of dilute urine Schlayer gave the name "tubular" hyposthenuria. The other type of abnormal chloride excretion occurred in experimental nephritis, where the tubules were normal but where the vessels were hypersensitive to stimulation. As a result the diuretic action of the salt was marked, and the added salt was excreted in an excess of fluid, its concentration remaining low and the specific gravity of the urine remaining unchanged. Schlayer called such a dilute urine "vascular" hyposthenuria. Both types of chloride excretion were found to occur clinically.

The length of time required by the kidney to excrete 500 mg. of potassium iodide given by mouth served as a criterion for the iodide test. Janeway⁷ has pointed out that this depends upon the qualitative reaction which is used to determine the presence of iodine in the urine. Schlayer selected Sandow's test and considered sixty hours normal, while von Monakow,⁸ taking starch paste and nitric acid, made forty-four hours the upper limit.

By using these various tests, Schlayer claims to be able to distinguish certain types of acute and chronic nephritis and to find their distinguishing characteristics to be sharply demarcated. Vascular nephritis, whether acute or chronic, is characterized by a delayed lactose excretion, by oliguria or polyuria, depending on the sensitiveness of the renal vessels, and by a normal chloride and iodide excretion. Tubular nephritis is shown by a normal water and lactose excretion, but with delayed chloride and iodide outputs. All grades of mixed functional disturbances are found between these two extremes. In a general way the tests point out

⁷ Trans. Cong. Amer. Phys. and Surg., 1913, ix, 14.

⁸ Deutsch. Arch. f. klin. Med., 1911, cii, 248.

the severity of the disease, and since they are all delicate, often show functional changes before clinical signs of nephritis develop. Schlayer has shown this prettily by observing cases over a long interval of time. He has been able to see cases with abnormal function by the tests later develop albuminuria, cylindruria, and hypertension. Repetition of the tests in such cases has demonstrated a progressively worse renal function with the increasing clinical severity of the disease. The work of Conzen,⁹ Eppinger and Barrenscheen,¹⁰ Rowntree and Fitz,¹¹ Herringham and Trevan,¹² Eisner,¹³ Michaud and Schlecht,¹⁴ and Frank and Benrenroth¹⁵ confirms the value of Schlayer's methods in the diagnosis of nephritis.

In regard to the anatomical changes producing the functional disturbances, however, there is a difference of opinion. Von Monakow found a delayed potassium iodide excretion when the salt excretion was undisturbed, and believed that disturbance of water excretion depended on tubular degeneration. Rowntree and Fitz considered lactose an index of the vascular condition of the kidney, but showed in the frog at least that the tubules in the absence of a glomerular system were capable of excreting the sugar. In summing up the relation of functional tests to pathological diagnosis in nephritis, Christian¹⁶ states that "so far too few cases are recorded with these functional tests and subsequent histological examination of the kidneys to justify final conclusions, but such as are recorded do not seem to indicate that any very close correlation between function and anatomical lesion can be made on the basis of the rate of excretion of such substances as lactose, potassium iodide, salt, and water."

Von Monakow, repeating Schlayer's work, added a nitrogen test to the others. This consisted in following the nitrogen balance during the period of observation, and on one day giving 20 gm. of urea, containing 9.3 gm. of nitrogen. According to his observations it was normally excreted within forty-eight hours, but was retained in nephritides with glomerular lesions. Although subsequent work has not proved the place of its excretion, there seems little doubt at present that the kidney has selective excretory capacities. The excretion of lactose, water, and nitrogen differs from that of sodium chloride and potassium iodide. By following the excretion of these substances and by adding test amounts it is possible to discover an abnormal renal function before marked clinical signs of kidney disease are manifest. The different types

⁹ Deutsch. Arch. f. klin. Med., 1912, cviii, 353.

¹⁰ Wien. med. Woch., 1912, lxii, 1408, 1497.

¹¹ Arch. Int. Med., 1913, xi, 121; *ibid.*, 258.

¹² Quart. Jour. Med., 1913, vi, 505.

¹³ Deutsch. Arch. f. klin. Med., 1913, cxii, 442.

¹⁴ Jahreskurse, f. ärztl. Fortbildung, 1913, iv, 3.

¹⁵ Verh. des Cong. f. innere Med., 1913, xxx, 217.

¹⁶ Trans. Cong. Amer. Phys. and Surg., 1913, ix, 1.

of functional disturbance are well illustrated by the following cases:

CASE I.—Tubular nephritis. Peter Bent Brigham Hospital. Medical No. 782.

A man, aged forty years, came to the hospital with acute articular rheumatism. His history was unimportant except for a previous attack of rheumatic fever. Three months ago he became unconscious while at work, remaining in this condition for four days. No paralysis was noted at the time. He made a normal recovery.

At entry, physical examination showed an enlarged heart. There was a faint systolic murmur at the apex. The aortic second sound was accentuated. The systolic blood-pressure was 185. There was moderate thickening of the peripheral vessels, and the urine showed a trace of albumin with occasional casts. The fundi oculorum were normal. There was no edema.

At the time the tests for renal function were made the acute stage of rheumatic fever had passed. The results of the functional tests are charted below.¹⁷

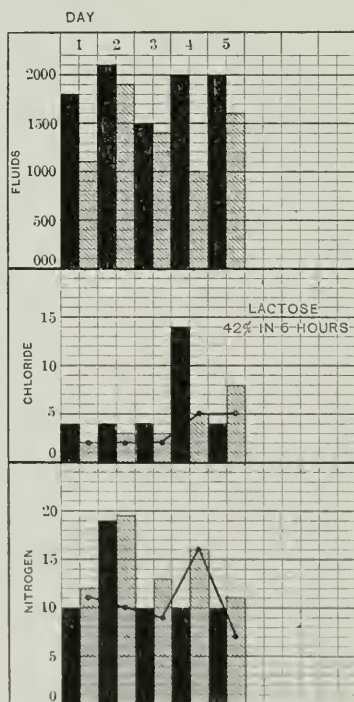


CHART I.—"Tubular" nephritis.

¹⁷ The black column in the accompanying charts represents intake, the cross-column output, the dotted lines the concentration of chloride or nitrogen per 100 c.c. of urine.

While the functional findings are not absolutely typical the striking feature is retention of chloride and water when added salt was given, while added nitrogen is excreted normally. This suggests tubular involvement. On the other hand the lactose excretion is somewhat delayed, and therefore vascular function must be interfered with to a certain extent. The case is called "tubular" because it illustrates with more than usual distinctness the type of excretion which characterizes abnormal tubular function.

CASE II.—Vascular nephritis. Peter Bent Brigham Hospital. Medical No. 131.

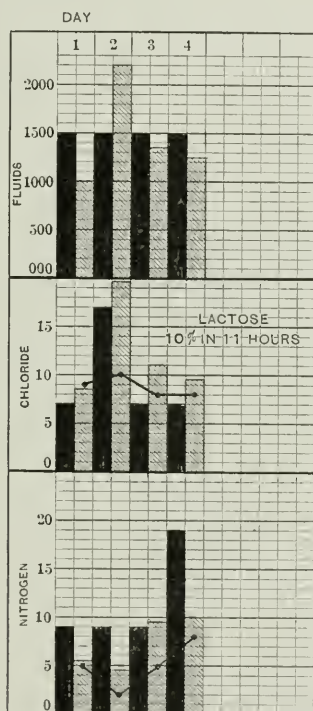


CHART II.—"Vascular" nephritis.

A woman, aged thirty years, entered the hospital complaining of "shortness of breath." As a girl she had scarlet fever and "convulsions." Ten years ago she noted shortness of breath on exertion. Two years ago her face and eyes were swollen at times. During the past year her physician had observed a high blood-pressure. On two or three occasions during this time she had mild convulsions, from which she recovered quickly. There was more or less headache.

Physical examination showed marked cardiac hypertrophy. There was a systolic murmur at the apex, and another of different pitch and intensity at the base. The aortic second sound was accentuated. The systolic blood-pressure was 200. The urine showed albumin and casts. The specific gravity was between 1010 to 1015. Fundus examination showed edema and hemorrhage of the disks without exudate.

In this case the vascular system was especially at fault. The lactose and nitrogen were poorly excreted. The tubules were able to increase the concentration of chloride, but the salt acted mainly as a diuretic, increasing the urinary output markedly. Thus the vessels were hypersensitive and as the specific gravity showed a relative fixation during the period of observation, the functional findings are those of "vascular hyposthenuria."

CASE III.—Mixed nephritis. Peter Bent Brigham Hospital. Medical No. 75.

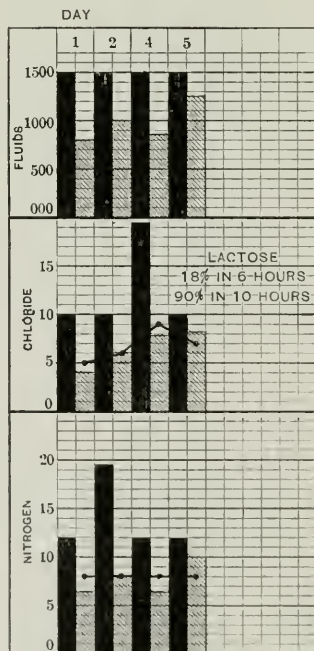


CHART III.—"Mixed" nephritis.

A painter, aged forty-five years, came to the hospital complaining of weakness of the arms and legs. His previous and family histories were negative. Physical examination gave signs of a peripheral neuritis, probably due to lead poisoning. In addition his heart was slightly enlarged, the aortic second sound was ringing, the

blood-pressure was 160, and the urine was of a fixed gravity, between 1014 to 1015, and contained albumin and casts. His renal functions were studied with the results shown above.

Here the function of both the tubules and vascular system was involved. There was a delayed lactose and nitrogen excretion; the vessels were insensitive to chloride stimulation. Salt concentration increased slightly, following the added amount, but not enough to increase the total output. Thus a mixed type of functional derangement was found, without a typical "vascular" or "tubular" hyposthenuria.

On the whole, Schlayer's tests are significant, chiefly because they show early functional disturbances in the kidney, and by repetition illustrate the rapidity of development of an early disease. But whether vascular and tubular function on an anatomical basis can be differentiated in Bright's disease with the same definition as in experimental toxic nephritis, remains to be determined by a careful study of more clinical and pathological material.

In advanced nephritis these tests are less useful. In the first place it is difficult to conceive of such a kidney in which pathological and functional lesions are not found in both tubules and vascular system to so great a degree as to make differentiation of function impossible. In the second place, whatever disturbances are found may be identical with those occurring in an early disease, and so give little prognostic information. The latter point is well demonstrated by the cases quoted. The most advanced case to all clinical appearances was the one recorded as "vascular" nephritis. Yet by the tests the worst case functionally was the one which showed the "mixed" type of excretion, and occurred in a man who had no symptoms of kidney disease whatever. Therefore in advanced Bright's disease, tests which estimate the total renal function and which are directed to determining the cause of symptoms encountered are of more value than finer ones which attempt to study individual functions of different anatomical units of the organ.

It is generally agreed that the kidney is the main excretory channel of the body, and that retention of substances through faulty elimination may lead to toxic manifestations. Prevost and Dumas,¹⁸ in 1821, found an increase in the urea content of the blood after extirpation of the kidneys. From that time various observers have isolated specific substances from the blood of uremic patients which they have considered the cause of symptoms. But each body successively incriminated has been successively rejected. At present renal insufficiency or uremia is regarded as a complex intoxication arising from unknown causes. But the degree of renal insufficiency can be estimated in a variety of ways.

¹⁸ Quoted by Schöndorff, *Pflüger's Arch. f. d. ges. Phys.*, 1899, lxxiv, 307.

In phenolsulphonephthalein, Rowntree and Geraghty¹⁹ have given the most valuable single aid to the estimation of total renal function, which is known at present. Phenolsulphonephthalein is a dye devoid of toxicity, and is eliminated from the body almost entirely through the kidney. Rowntree and Geraghty have shown from careful studies in nephritis that the amount of phthalein excreted varies in direct proportion to the severity of the disease. In fatal uremia only traces of the dye are found in the urine, while in mild nephritis the amount recovered is nearly normal. In cardio-renal disease where the heart is chiefly at fault and the kidneys are congested without a marked nephritis a low phthalein output may be observed at first, rapidly rising as the circulation is restored, while if a severe nephritis is present no change in the phthalein excretion accompanies the improved circulation.

In addition to its accuracy the test has the added advantages of being rapid and so simple that it may be used by the general practitioner. A solution of phenolsulphonephthalein is made containing 6 mg. of the dye to 1 c.c. of salt solution. This is injected either intravenously or intramuscularly under aseptic conditions. Following the injection all the urine excreted is collected at the end of one hour and two hours, is diluted to a suitable amount with alkaline water, and its phthalein content is estimated by colorimetry. The Du Boseq colorimeter may be used or the simpler Autenrieth-Königsberger machine or even a series of test-tubes containing varying amounts of the dye in varying dilutions. If the colorimeter is used a standard solution for comparison is made which contains 6 mg. of phthalein in a liter of alkaline water. Normally from 40 to 60 per cent. of the amount injected is recovered in one hour, and from 60 to 80 per cent. in two hours following intramuscular injection. The test has been used successfully by so many observers that its value must be accepted as a fact.

In a few cases, however, the excretion of the dye gives unreliable information. This appears to be because a diseased kidney may be hyperpermeable to one substance, while it is impermeable to another. Thus it may be permeable to a dye and impermeable, possibly, to an unknown poison causing certain symptoms of the disease. Bard and Bonnet,²⁰ in studies on renal function in which potassium iodide and methylene blue were used as tests, found that in interstitial nephritis the excretion of both substances was faulty, in "epithelial" nephritis the kidney was hyperpermeable for both, and in secondary interstitial nephritis the methylene-blue excretion was normal or increased, while that of potassium iodide was diminished. Pepper and Austin²¹ have lately called attention to a case of nephritis with marked albuminuria, cylindruria, and

¹⁹ Jour. Pharm. and Exp. Ther., 1909, i, 579; Arch. Int. Med., 1912, ix, 284.

²⁰ Arch. Gén. de Méd., 1898, 3d ser., ix, 129, 283, 464.

²¹ AMER. JOUR. MED. SCI., 1913, cxlv, 254.

edema in which the phthalein output was normal, and Baetjer²² reports nearly similar cases. Foster²³ illustrates the difficulty of prognosis by the use of any one kind of functional test giving as examples cases which died of uremia with a practically normal phthalein output shortly before death. In this regard the following case is of interest.

CASE IV.—Peter Bent Brigham Hospital. Medical No. 4.

A woman, aged sixty-three years, was admitted to the hospital with a history of dyspnea of one year's duration. Her family and previous histories were negative. Her habits were good. Two months before entry her eyesight had failed, and she began to have mild occipital headaches. Physical examination was unimportant except for marked cardiac hypertrophy, an apical systolic murmur, an increased blood-pressure (232 mm. systolic), and a urine which contained albumin and casts. She appeared to be a case of advanced interstitial nephritis, confirmed by a phthalein excretion of 12 per cent. for two hours. Rest in bed produced no benefit. In two weeks she became drowsy and was bled. On the following day the phthalein excretion was 30 per cent. for one hour and twenty minutes. Her general condition did not improve. A week later she became comatose and put out only traces of phthalein in two hours. She was bled again. She became brighter temporarily, and her phthalein excretion on the next day was 54 per cent. for two hours. She lapsed into coma soon and died shortly. On the day of her death she put out 8 per cent. of phthalein in two hours. Autopsy showed typical contracted kidneys. It is difficult to explain this rapid premortal rise in the excretion of phthalein on any other ground than that bleeding had in some way rendered the kidney hyperpermeable to the dye without having any definite influence on the disease.

But, on the whole, the phthalein test is of great value. These latter observations merely emphasize that to judge the degree of renal insufficiency with accuracy more than one test must be used.

Of substances studied in the blood of nephritics the concentration of the incoagulable nitrogen and urea has been found to be of most importance. Folin and Denis²⁴ and Marshall²⁵ have recently devised relatively simple methods for performing these analyses, making possible such estimations as a matter of routine in hospitals with well-equipped laboratories. In regard to the technique employed, readers are referred to the original articles. The older methods required large amounts of blood, and were time-consuming. Nevertheless, Ascoli,²⁶ Strauss,²⁷ and others found in severe grades

²² Arch. Int. Med., 1913, xi, 593.

²³ Arch. Int. Med., 1913, xii, 452.

²⁴ Jour. Biol. Chem., 1912, xi, 527.

²⁵ Ibid., 1913, xv, 487.

²⁶ Pflüger's Arch. f. d. ges. Phys., 1901, lxxvii, 103.

²⁷ Die Chronische Nierentzündungen in ihrer Einwirkung auf die Blutflüssigkeit und deren Behandlung, Berlin, 1902, A. Hirschwald.

of nephritis the nitrogen usually though not invariably increased, the increase being much more marked toward death. Obermayer and Popper²⁸ showed that cases of uremia have a higher incoagulable nitrogen content in the blood than do normal individuals or cases of nephritis without uremia, and that of this nitrogen the urea fraction increases with the development of intoxication. Widal²⁹ has gone so far as to believe that it is possible to base an approximate prognosis as to length of life on the degree of urea retention.

Opposed to this, Strauss,³⁰ in a recent paper, describes different clinical types of uremia, and says that high values for blood-nitrogen are usually accompanied by uremic manifestations, but that a low concentration for nitrogen does not mean a favorable outcome for the disease, because fatal uremia may develop when low figures are present as well as when high figures are found. Foster's results bear out this statement. Thus this test is not infallible, and proves again that to judge accurately the degree of renal insufficiency more than one test for renal function must be made.

The relation of faulty sodium chloride excretion to edema in nephritis and its independence of nitrogen retention has been proved by Widal,³¹ although Bickel³² in a series of analyses was unable to find any relationship between the development of uremia and the amount of chloride accumulation in the blood as estimated by electrical conductivity. The apparent contradiction of faulty chloride elimination without an increase of its blood-concentration has been explained by two hypotheses. Bohne,³³ by determining the chloride content of nephritic organs at autopsy in a limited number of cases, believed that the salt was stored in the tissues rather than in the blood, while Marie³⁴ has assumed that in nephritis, chlorides are retained in a "free" state where they increase the concentration of the blood and tissues, and in this way produce accumulation of fluid or circulate as a "fixed" compound when they are inactive. Whatever the relation of salt retention to edema may be, there is no doubt that certain cases of advanced nephritis with normal function in other regards are unable to excrete sodium chloride and develop edema. The cases reported by Austin and Pepper and by Baetjer show this strikingly. In Baetjer's cases, which were of well-marked nephritis, the phthalein and lactose outputs were normal or increased; yet the patients were unable to excrete chloride, and after its administration retained water. Apparently Austin and Pepper's case is of the same type. This

²⁸ Ztsch. f. klin. Med., 1909, lxxvii, 332.

²⁹ Bull. et mém. d. hôp. de Paris, 1911, series 3, xxxii, 627.

³⁰ Deutsch. Arch. f. klin. Med., 1912, cvi, 219.

³¹ Verh. des. Cong. f. innere Med., 1909, xxvi, 43.

³² Deutsch. med. Woch., 1902, xxviii, 501.

³³ Fortschr. der Med., 1897, xv, 121.

³⁴ Sem. Méd., 1903, xxiii, 385.

shows from another point of view that more than one kind of test must be made to estimate the total renal function.

Finally, there is considerable evidence at hand that certain manifestations of renal insufficiency are produced by the retention of acids in the body, with a consequent acidosis. This can be measured by direct determination of blood-alkalinity, by following the carbon dioxide tension of expired air, since it has been shown to be diminished in various acidoses, or by determining the urinary acidity. Older methods for determining blood-reaction based upon its direct titration against normal acids are inaccurate. Nevertheless, von Jaksch,³⁵ in 1888, found the reaction of the blood abnormally acid in uremia, and this was confirmed by Peiper³⁶ and Orlowski.³⁷ Brandenburg³⁸ compared the nitrogen of the blood with its reaction in a variety of cases, and made the interesting observation that in uremia there was often an acidosis which bore no relation to the degree of nitrogen retention. While these observations are not beyond criticism, the recent work of Straub and Schlayer,³⁹ and of Porges and Leimdörfer⁴⁰ proves that the results obtained are important. Working with Haldane's instrument, these observers have noted independently a lowering of the carbon dioxide tension in uremic cases, concluding that the condition has to do with acidosis. Sellards,⁴¹ Palmer,⁴² and Palmer and Henderson⁴³ have considered an increased urinary acidity as another sign of acidosis, and have found it a frequent occurrence in nephritis.

All these observations show that the study of renal function in advanced nephritis is extremely complex. A diseased kidney affords as varied a picture in regard to its functional diagnosis as it does in regard to its clinical manifestations. None of the tests, alone, which have been considered, justify a definite estimate of the renal function in every case, nor has their relationship to each other and to the clinical and pathological condition associated with them been controlled in a sufficient number of cases to establish their real meanings. There is no doubt, however, that a variety of tests for renal function helps to make a diagnosis of kidney disease before definite signs of nephritis manifest themselves, and affords accurate information in regard to prognosis by estimating the degree and type of renal insufficiency. Moreover, a series of such tests is of help in treatment.

Widal⁴⁴ believes that three distinct symptom complexes occur

³⁵ Ztschr. f. klin. Med., 1888, xiii, 350.

³⁶ Virchows Arch., 1889, cxvi, 337.

³⁷ Cent. f. Stoffw. v. verd. Krankh., 1902, iii, 123.

³⁸ Ztschr. f. klin. Med., 1899, xxxvi, 267.

³⁹ Münch. med. Woch., 1912, lix, 568.

⁴⁰ Ztsch. f. klin. Med., 1913, lxxvii, 464.

⁴¹ Johns Hopkins Hosp. Bull., 1912, xxiii, 289.

⁴² Boston Med. and Surg. Jour., 1913, clxix, 464.

⁴³ Jour. Biol. Chem., 1913, xiii, 393; Arch. Int. Med., 1913, xii, 146.

⁴⁴ Le Mouvement Médical, 1913, i, 1.

in cardiorenal disease. Patients with high blood-pressure suffer from one train of symptoms which include circulatory disturbances, like tinnitus, vertigo, headache, cerebral hemorrhage, or cardiac decompensation. Patients with chloride retention suffer from equally characteristic symptoms. Here edema is the underlying factor. The digestive, nervous, or respiratory organs may be affected, depending on the situation of the edema, with diarrhea, delirium and convulsions, or dyspnea. Patients with nitrogen retention do not develop edema, but show albuminuric retinitis, a progressive loss of appetite, anemia, and coma. Such individuals are subject to ulcerative gastro-enteritis, pleuritis, or pericarditis. Naturally the symptoms become intermixed in advanced cases, so that a sharp division is impossible. But Widal considers that in the "hypertensive" cases the heart must be watched, in the chloride retention cases with edema, a salt-poor diet is indicated, and that the nitrogen retention cases are the most severe and hopeless.

Such a dogmatic division of symptoms in cardiorenal disease needs confirmation. But a rational diet based upon the kidney's selective excretory capacity can be instituted by following the excretion and blood-concentration of nitrogen, salt and water. Von Noorden⁴⁵ has formulated general rules for the protective treatment of nephritis. A case can be treated on a less empirical basis, and more as an individual by making these simple tests. It is fair to assume that cases unable to excrete chloride should be given a salt-poor diet; cases unable to excrete nitrogen and with nitrogen accumulation in the blood should be given low protein diets, and cases of acidosis with normal functions in other respects should receive alkalis.

For these reasons, tests for renal function in Bright's disease are important for diagnosis, prognosis, and treatment. The lactose, salt, water, potassium iodide, and nitrogen tests are of special value in the early diagnosis of nephritis. In advanced nephritis the functional condition is so complex that tests to estimate total function are more useful than those designed to study the function of different parts of the kidney. The phthalein excretion is the most satisfactory single test. The non-protein nitrogen of the blood offers additional information in regard to faulty eliminative powers on the part of the kidney. Yet cases occur in which both blood-nitrogen and phthalein are normal, and chloride retention is an important factor in the disease. Finally, acidosis has been shown to exist in uremia. Since no one test is perfect in determining total renal function, cases must be studied from several points of view. A rational dietetic treatment can be given in individual cases based on the conditions disclosed by the study of the kidney's selective excretory capacity.

⁴⁵ Metabolism and Practical Medicine, Chicago, 1907, ii, 433.

OBSERVATIONS ON THE INTRAVENOUS USE OF STROPHANTHIN WITH REGULAR AND IRREGULAR PULSE RHYTHMS.

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SINCE Fraenkel,¹ in 1906, reported the value of intravenous injections of strophanthin in heart failure—noting increased amplitude and slowing of the pulse, together with diuresis—observations on the intravenous use of this drug with favorable results have followed in considerable numbers from other writers. However, these observations have not been explicit as to the type of cases in which strophanthin was employed, and until the more recent reports of Agassiz² and Linnell,³ have produced the impression that it yielded beneficial results in all cases of heart failure, regardless of the pulse rhythms. This is clearly not so, and the type of cases in which good results are obtained is so sharply defined that it would seem to deserve more emphasis than it has generally received.

The present report is made with the object of studying further the nature and duration of the actions of strophanthin in cardiac lesions, with particular reference to the pulse rhythm present, since this feature decides how effectual the injections will prove. The work of Mackenzie⁴ has made clear that digitalis and its allies produce their striking results in a clearly marked group of clinical cases. Definite slowing of the pulse under digitalis occurs in the presence of the *pulsus irregularis perpetuus* and the ventricular form of venous pulse, the complex familiar as auricular fibrillation. In conditions other than auricular fibrillation it produces also at times a slowing of the pulse that is more apparent than real and occasionally to the disadvantage of the patient. It is a matter of record that digitalis administration in the presence of a normal regular pulse rhythm may produce for the time being, and sometimes permanently, any of the commoner irregularities of the heart, such as premature contractions, phasic variations, heart-block, *pulsus alternans*, and auricular fibrillations (Fig. 1). Frequently, too, the finger is taken as a guide to the slowing of the pulse in these instances, and may readily lead to erroneous conclusions, since an apparently long interval between pulse waves may be due to a weak contraction perceptible at the

¹ Fraenkel, *Verhand. d. Kongress f. innere Medizin*, 1906, xxiii, 257.

² Agassiz, C. D. S., *Observations on the Effect of Strophanthin in Cases of Auricular Fibrillation*, Heart, vol. iii, No. 4, p. 353.

³ Linnell, J. W., *The Use of Strophanthin Administered Intravenously in Cases of Heart Disease*. Publication printed for private circulation, London, 1913.

⁴ Mackenzie, James, *Digitalis*, Heart, vol. ii, No. 4.

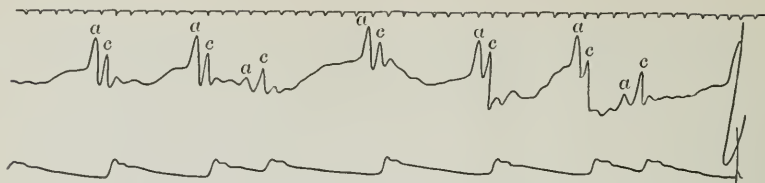


FIG. 1 (a).—Marked sinus arrhythmia induced by digitalis in a previously regular pulse.

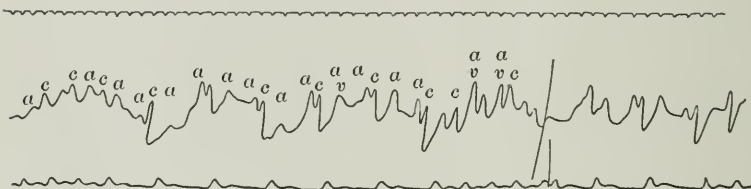


FIG. 1 (b).—Heart block occasioned in a previously regular pulse by digitalis (septic endocarditis).

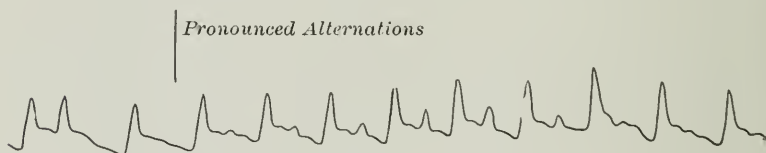


FIG. 1 (c).—Pulsus alternans.

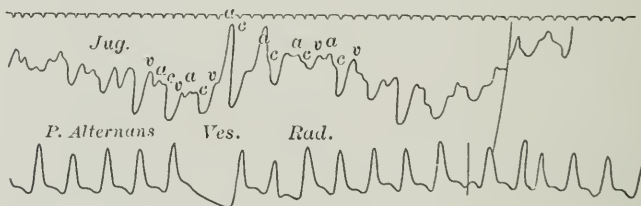


FIG. 1 (d).—Ventricular extrasystole induced in a previously regular pulse after a total administration of 15ij tinct. strophanthus.

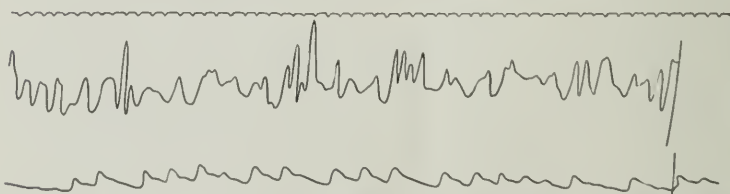


FIG. 1 (e).—Auricular fibrillation (permanent) induced after 1xxx tinct. digitalis. Case of Dr. J. D. Heard.

FIG. 1.—Illustrating irregularities brought on in previously regular pulse rhythms by the administration of digitalis and strophanthus. Time marked in all cases in one-fifth second.

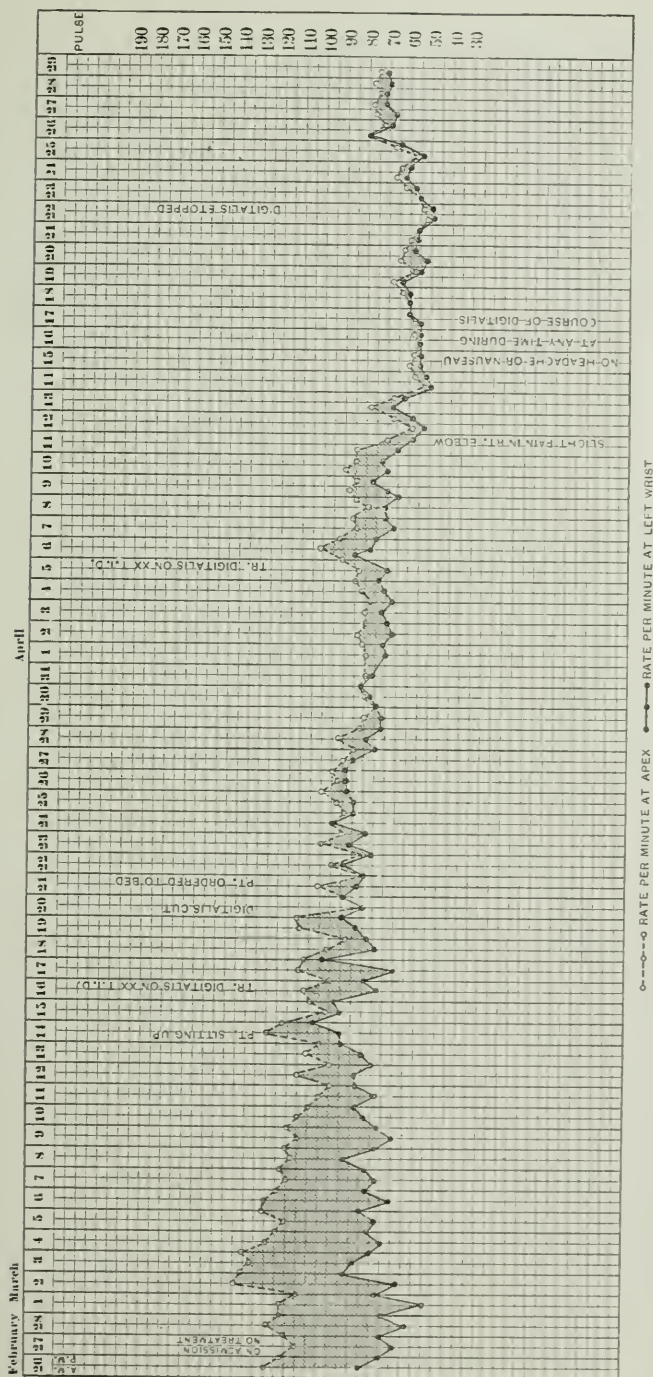


FIG. 2.—Showing diminution of pulse deficit after digitalis administration in auricular fibrillation. Upper level, Lower level, pulse at wrist.

apex but too feeble to reach the wrist. The same holds true to even a greater degree in auricular fibrillation, as is commonly attested by most clinical charts, the pulse rate as recorded by the nurse being many counts below the actual heart beat. This difference in rate between apex and radial pulse—the pulse deficit—may, as pointed out by James and Hart,⁵ be made a guide to the patient's improvement, since it progressively grows less or even disappears under treatment (Fig. 2).

In the present observations the pulse has been termed irregular in the presence of a disorderly rhythm with no two beats alike in length or amplitude, and a positive venous pulse, and regular if there is evidence of an underlying, orderly arrangement of contractions, even though these be interrupted by contractions of atypical origin. In all, twenty cases with regular and irregular pulse rhythms were studied. Those having regular rhythms were all clearly defined, and showed no intercurrent irregularities.

PREPARATIONS USED AND DOSAGE. Two forms of strophanthin were used, and, so far as could be judged, showed no difference in efficiency—the ampoules of Boehringer containing 1 mg. each, or $\frac{1}{60}$ gr., and the tablets of Burroughs, Welleome & Co., of $\frac{1}{500}$ gr. each, dissolved in sterile water. As a rule $\frac{1}{60}$ gr. was employed. A dose of less than $\frac{1}{120}$ gr. did not prove practicable, and, except in one instance that will be mentioned, we saw no ill effects from $\frac{1}{60}$ gr. The smaller the dose the more frequently it may be employed, but since the procedure is not a painless one, it seemed always desirable to give at one time the largest dose within the limits of safety. A dose of $\frac{1}{60}$ gr. should, and need, scarcely be repeated in less than forty-eight hours.

The injection was made with a hypodermic syringe into a vein at the bend of the elbow, the arm having been surgically cleansed and a tourniquet applied. It is important after introducing the needle, and before pressing the plunger, to see that blood is flowing into the syringe so as to make sure that none of the injection enters the subcutaneous tissues and causes a cellulitis. In two cases a red, swollen, tender arm resulted from some of the strophanthin escaping into the subcutaneous tissues, the symptoms subsiding after three or four days. One case, already *in extremis*, had her death hastened by what must have been too great a dose for her body weight. Otherwise, no ill effects were noted, such as rigors, headaches, and rises of temperature, which some observers have reported.

EFFECT ON THE HEART RATE AND ITS DURATION. In those cases which reacted, slowing of the pulse rate occurred within twenty minutes, though in some instances a maximal effect was not obtained for six to eight hours. Where a sufficient dose was

⁵ James and Hart, Auricular Fibrillation, Clinical Observations on Pulse Deficit, Digitalis, and Blood-pressure, AMER. JOUR. MED. SCI., January, 1914, p. 63.

injected to obtain a maximal slowing, the pulse did not begin to accelerate again for three to ten days. The duration of the effect seemed to be proportionate to the extent of slowing rather than to the dosage employed, as already noted by Agassiz.⁶

OTHER EFFECTS. Where the subjective symptoms are urgent, the effect of strophanthin in suitable cases is most striking. Coughing and dyspnea cease within a few minutes, and the patient experiences a relief comparable in its rapidity only to that obtained from morphine, while the heart rate is sufficiently lowered to tide him over until digitalis, administered orally, can produce its effects.

On the other hand, it was interesting to observe that an enlarged pulsating liver did not at once diminish in size, but retreated only after a number of days to its normal dimensions. Similarly, we could not observe any reductions in the heart outlines, either immediately or subsequently. Blood-pressure also was little affected, but showed a tendency to a moderate rise whenever decisive slowing occurred. The cases which reacted decisively did not, except in one instance, revert to a regular rhythm, but continued to fibrillate at a lower rate.

CASES STUDIED. Of the 20 cases in this series, 10 showed the pulsus irregularis; in 9 of these it was constant, in 1 it interrupted the normal rhythm in paroxysms; 10 cases had at all times a regular, rapid pulse, 9 of these being an acceleration of the normal pacemaker rhythm; 1 being a case of paroxysmal tachycardia of auricular origin.

With one exception all the cases studied showed a valvular lesion, with accelerated pulse. In the one exception there was pulse acceleration without cardiac lesion in a postoperative laparotomy, terminating fatally.

Of the cases with pulsus irregularis, 6 had a rapid pulse (in all cases over 100) and slight dyspnea, but no further symptoms. The other 4 were seriously ill. The reaction in all cases was decisive, the pulse rate dropping from 20 to 60 beats per minute, the maximum of reaction being reached in twenty minutes to eight hours. In one instance, where three doses of $\frac{1}{120}$ gr. were given during a week, the maximal reaction did not occur until one hour after the final injection (Fig. 3).

Of the 4 serious cases, 1 on the service of Dr. James D. Heard, at St. Francis' Hospital, afforded very striking results. This case has been reported in detail.⁷ It will suffice to say that from a condition of extreme dyspnea with a totally irregular apex beat of 164, pulmonary congestion, enlarged pulsating liver, and great edema of the lower extremities, the patient was brought in twenty minutes after the injection of $\frac{1}{120}$ gr. to a condition of

⁶ Loc. cit.

⁷ Cohn, A. E., and Heard, James D., A Case of Auricular Fibrillation with Post-mortem Examination, *Archives of Internal Medicine*, June, 1913.

comfort, with an apex beat of 116. Four hours later a second injection of $\frac{1}{120}$ gr. was given, bringing the pulse to 100, after which the oral administration of digitalis was begun.

Two instances of pulsus irregularis occurred in association with pneumonia. In both instances the irregularity antedated the pneumonia—in the first by ten years and in the second by three. There was a severe toxemia. In the first case $\frac{1}{120}$ gr. of strophanthin reduced a pulse of 160 to 80 in one hour. In the second case the same dose caused a drop from 144 to 92 in the same time. Notwithstanding the strikingly favorable results as to the cardiac mechanism, both cases pursued their unfavorable course to a fatal termination.

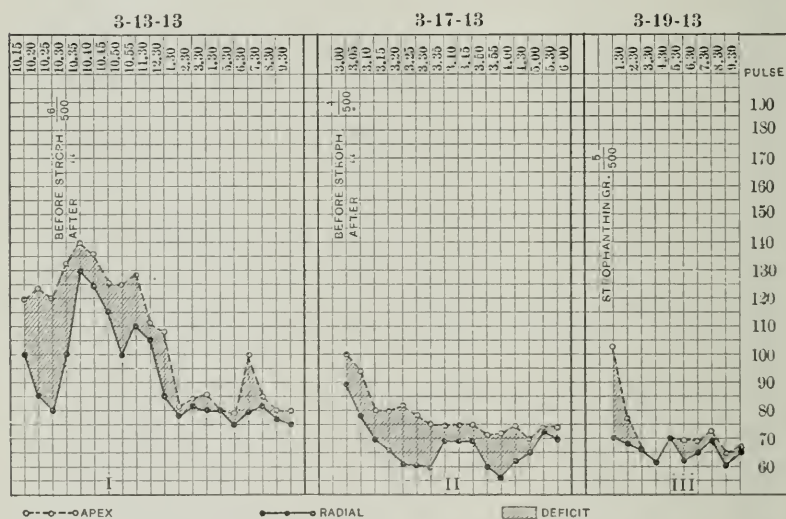


FIG. 3.—Showing progressive lowering of apex rate and pulse deficit by repeated injections of strophanthin.

The last case with occasional pulsus irregularis occurred on the service of Dr. R. T. Miller, Jr., at St. Francis' Hospital, where he had been admitted for a gall-stone operation. One paroxysm of pulsus irregularis occurred before operation, but terminated spontaneously. Two others occurred after operation, with an apex rate of 140 and great distress. In each postoperative instance the normal rhythm, at a rate of 76, was resumed within one-half hour after administering $\frac{1}{120}$ gr. strophanthin. However, it is difficult to say how far these injections were responsible for any improvement in view of the spontaneous termination of the first attack.

CASES PRESENTING A REGULAR RHYTHM. Of 10 cases with regular pulse rate, 3 showed a definite slowing, though in all the circumstances were such as to make them exceptional cases. One,

a case of advanced decompensation, showed for a few minutes only a drop in rate of 14; in one the rate fell to half of what it had been a few moments before, but this was speedily followed by a rise in rate and a fatal termination; and another, with paroxysmal tachycardia of auricular origin, resumed its normal rate. Seven were unaffected (Fig. 4).

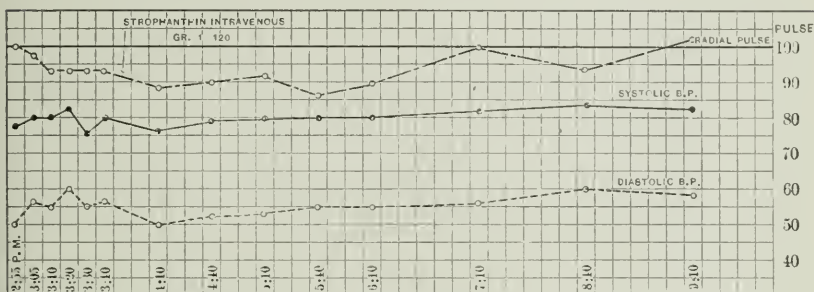


FIG. 4.—Case I. R. B. (regular rhythms). Showing action of $\frac{1}{26}$ gr. strophanthin. Effect very slight and transitory.

The cases reacting, all of them atypical, were as follows:

1. *Paroxysmal Tachycardia of Auricular Origin.* When first seen the attack had been going on for twelve days. Apex rate, 208 per minute and regular. Skin and mucous membranes moderately cyanotic, veins of the neck distended and fluttering rapidly. Heart one and one-half inch to the right and four inches to left of midline in the third interspace, with faint tic-tac sounds and no murmurs. Liver a trifle below the costal border; slight pitting of the skin over the tibiae. Twelve days after the onset of this attack gr. $\frac{1}{60}$ strophanthin was injected, with no effect on the pulse rate. Eleven days later, the twenty-third day of the attack, gr. $\frac{1}{60}$ strophanthin was again administered at 9.30 P.M. One hour later there was no change, but when next seen at 8 A.M. the following morning the pulse was found to be 84, and remained at this rate thereafter. The patient volunteered the information that at midnight, following the injection, he had felt a sudden relief. Here again it is difficult to say whether the sudden relief was due to strophanthin or whether it was given coincidentally with the spontaneous cessation of the paroxysm.

2. A patient, aged sixteen years, female, with mitral insufficiency and advanced decompensation, pulse rate 104 and regular, was given gr. $\frac{1}{60}$ strophanthin. In two hours the pulse rate had dropped to 84, but remained so only for a little while, and rose again steadily until her death, which occurred on the same day.

3. *Overdosage.* The patient, a colored girl, aged fourteen years, suffering with acute articular rheumatism, endocarditis, and pericarditis; pulse rate 124, regular rhythm. Weight eighty pounds;

$\frac{1}{60}$ gr. strophanthin was administered at 11 A.M. At 11.15 the pulse was 64 and of an irregular rhythm not determined, as there was no time to apply a polygraph. Immediately after, Cheyne Stokes breathing ensued, the pulse rate rose again to 110, and at 11.30 death occurred. In this case the dose was too great in proportion to her body weight and her serious condition. Though death seemed impending, there is no doubt that the strophanthin injection materially hastened it.

CONCLUSIONS. 1. The action of strophanthin administered intravenously is similar to that of other members of the digitalis group administered orally, but far more rapid.

2. Strophanthin had, in this series, a decisive effect in all cases with *pulsus irregularis perpetuus*. Where the pulse rhythm was regular, it showed an effect in only three instances out of ten, and this was both slight and transitory, except for the case of paroxysmal tachycardia.

3. In desperate cases of the *pulsus irregularis perpetuus* type, strophanthin administered intravenously will tide the patient over until digitalis, orally administered, has time to take effect.

4. In cases of the *pulsus irregularis perpetuus* type, the first effects are noted in twenty to thirty minutes, though the maximum may not be apparent for seven or eight hours. This effect lasts from three to ten days.

5. It does not seem advisable to give on any one occasion more than gr. $\frac{1}{60}$, and this, if repeated, should not be done before forty-eight hours; $\frac{1}{120}$ gr. has given a maximum result. On the other hand it may sometimes take more than $\frac{1}{60}$ gr. to produce this.

6. Two cases of paroxysmal tachycardia are reported with strophanthin administration, both followed by cessation of the attacks. It is not clear, however, to what extent the strophanthin was responsible for this phenomenon.

REPORT OF CASES WITH IRREGULAR RHYTHM.

CASE I.—Mitral stenosis; auricular fibrillation. Mrs. T. G. (service of Dr. James D. Heard, St. Francis Hospital), white, aged thirty-seven years. Complained of shortness of breath and cough. A previous history of chorea and acute rheumatic fever. On admission she had a diffuse precordial heave—a rough vibrating thrill—and a soft presystolic murmur rising in crescendo to a booming first sound. Pulmonic second sound greatly accelerated. Pulse was regular in rhythm and 120 to the minute. Lower border of the liver two and one-half inches below the costal margin. No edema. After two doses of $\mathfrak{M}\mathfrak{xv}$ each of tincture of digitalis, she suddenly developed auricular fibrillation, which continued until her death five months later. After a few weeks she was discharged, with a pulse rate of 90 and feeling comfortable.

Two months later she returned to the hospital in an alarming state of decompensation—extensive swelling of the legs and abdomen, extreme orthopnea, a cough with frothy blood-tinged expectoration, and an irregular pulse of 160 to the minute, small and thready. The lower border of the liver extended 3 inches below the costal margin. There was marked congestion of the pulmonary bases and the heart sounds too tumultuous to analyze.

At 11 A.M. on the day after her second admission she received $\frac{1}{120}$ gr. strophanthin. Apex rate at this time was 160 per minute. At 11.30 her apex rate had dropped to 104 per minute and she was feeling comfortable. At 3.30 P.M. she received another dose of gr. $\frac{1}{120}$, bringing her apex rate in thirty minutes more to 100 per minute. At this time digitalis was administered by mouth and her lowered heart rate continued, aided by this oral administration. She left the hospital one month later in comfortable condition and with a heart rate of 84. The edema of her extremities and her engorged liver did not at once recede, but diminished slowly during the ensuing month.

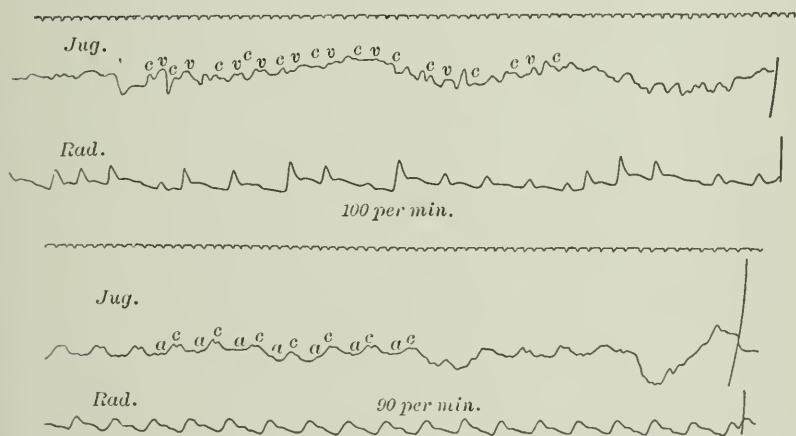


FIG. 5.—Case II (normal rhythm). Mr. S. Showing spontaneous reversion from auricular fibrillation to normal rhythm before operation.

CASE II.—S., male, white, aged sixty years; gall-stones; myocarditis; auricular fibrillation occurring in paroxysms. Patient was admitted for cholecystotomy. Pulsus irregularis; heart rate of 100. After three days in the hospital his heart suddenly reverted to a normal rhythm, with a pulse rate of 90. There was nothing in his treatment to explain this, save an unusually effectual enema.

Operation ensued and was successfully completed without any unfavorable results. Twenty-four hours after, he became dyspneic and cyanotic, and he again showed auricular fibrillation, with a heart rate of 144. $\frac{1}{120}$ gr. strophanthin was at once administered intravenously. Within an hour the pulse rate had dropped to

80 and, moreover, had resumed a regular rhythm. It remained so until the next day, when auricular fibrillation again was inaugurated, with extreme distress. A similar dose was again injected and a drop not only to the normal rate, but rhythm as well ensued within an hour and remained so until his discharge from the hospital in good condition one month later (Fig. 5).

CASE III.—G. F., white, male, aged fifty-four years. Mitral insufficiency; myocarditis, auricular fibrillation.

The patient, an attorney, when seen had had an irregular heart action with dyspnea on exertion for four years, but had been incapacitated for only the past four months. The apex rate was 168, with slight pulmonary congestion, but no signs of congestion in other organs.

Strophanthin gr. $\frac{1}{120}$ given intravenously resulted in a drop to 120 within one and one-half hours. No further strophanthin was given, and the heart remained at this rate for three days, when digitalis orally administered on the first day in doses $\frac{1}{5}$ j per day began to take effect, and one week from the time that he was first seen the heart rate was 78 and the general condition so improved that he wanted to return to work.

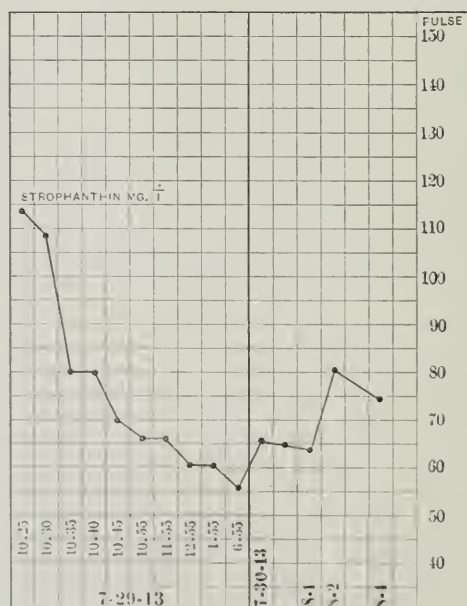


FIG. 6.—Auricular fibrillation. Case IV. Showing pronounced and rapid effect of injection of $\frac{1}{120}$ gr. strophanthin. The curve represents the apex rate.

CASE IV.—S. L., female, white, aged twenty years. Mitral insufficiency and auricular fibrillation.

She never had rheumatism or chorea, but had suffered with a number of attacks of sore throat. Three years ago she began to complain of shortness of breath on the slightest exertion, which has continued with slight remission ever since.

On admission her heart rate was 120 per minute, and totally irregular. There were no signs of secondary congestion, and she was only moderately dyspneic. At 10.25 A.M. she received $\frac{1}{60}$ gr. strophanthin intravenously. At 12.30 her heart rate had dropped to 60. A few hours later it had further dropped to 55 and did not begin to go up again until the third day afterward. Her condition remained comfortable throughout (Fig. 6).

CASE V.—C. G., Italian, male, aged fifty years. Myocarditis, with auricular fibrillation. During the previous three years he had had a number of attacks of multiple arthritic pains, but had never been laid up. In the past year there have been occasional attacks of shortness of breath. No further symptoms. Venereal history negative.

On admission, pulsus irregularis; heart rate 140. Heart outlines two and a half inches to the right and four inches to the left of the midline in the third interspace. Cardiac respiratory murmur present, but no actual heart murmurs. Moderate cyanosis. Very slight pitting over tibiae. Three injections of strophanthin were given (Fig. 3). March 13, $\frac{1}{80}$ gr. reduced the heart rate in three hours from 140 to 80, almost wiping out the pulse deficit. On March 17, the pulse having again risen to 100, $\frac{1}{120}$ gr. was administered with a drop to 75 in fifty minutes. On March 19, the pulse having risen again to 100, he was given a third injection of $\frac{1}{100}$ gr. with a drop in three hours to 68. He left the hospital one month later in excellent condition.

CASE VI.—J. D. (service of Dr. Nelson H. Clark, St. Margaret's Hospital), white, aged forty-four years. Myocarditis with auricular fibrillation. No history of rheumatic fever, chorea, tonsillitis, or any acute infection. Eight months ago, while at work, he became suddenly short of breath, and slight exertion since that time has brought on dyspnea.

RECORD OF TREATMENT.

		Apex.	Radial.	Systolic blood-pressure.
December 15,	9.45 P.M.	134	84	120
	10.05 P.M.		Strophanthin, gr. $\frac{1}{60}$	
	10.12	128	72	123
	10.17 P.M.	132	54	130
	10.22 P.M.	124	56	130
	10.27 P.M.	118	56	135
	10.35 P.M.	120	52	132
	10.45 P.M.	115	48	130

		Apex.	Radial.	Systolic blood-pressure.
December 16,	4.25 P.M.	126	52	121
	4.32 P.M.		Strophanthin, gr. $\frac{1}{120}$	
	4.38 P.M.	110	76	130
	4.43 P.M.	90	84	125
	4.50 P.M.	96	88	125
	5.00 P.M.	94	84	125
December 22,	2.36 P.M.	104	..	118
	2.41 P.M.		Strophanthin, gr. $\frac{1}{100}$	
	2.46 P.M.	100	..	128
	2.51 P.M.	88	..	130
	2.56 P.M.	88	..	134
	3.01 P.M.	88	..	134
	3.06 P.M.	80	..	134
	3.11 P.M.	76	..	137
	3.16 P.M.	80	..	134
	3.21 P.M.	82	..	134
	3.26 P.M.	84	..	134
	3.31 P.M.	80	..	138

CASE VII.—Miss R. (service of Dr. Nelson H. Clark, St. Margaret's Hospital), white, aged thirty-eight years. Mitral stenosis—auricular fibrillation—with a previous history of rheumatic fever. The patient was a small, frail woman, very wretched on account of the nervous discomfort produced by the sensation of fluttering about her heart. More frequent injections were used with her than with any other patient. They occasioned her such prompt relief that she used to ask for them.

		Apex.	Radial.	Systolic blood-pressure.
November 3,	4.30 P.M.	108		
	4.35 P.M.	118		
	4.45 P.M.	112		
	4.50 P.M.		Strophanthin, gr. $\frac{1}{80}$	
	5.00 P.M.	90		
	5.05 P.M.	88		
	5.13 P.M.	84		
	5.18 P.M.	78		
	5.25 P.M.	76		
	5.30 P.M.	76		
	8.00 P.M.	74		
	9.00 P.M.	82		
	10.00 P.M.	70		
	11.00 P.M.	80		
	12.00 P.M.	80		
November 20,	9.35 A.M.	132	96	65
	9.40 A.M.		Strophanthin, gr. $\frac{1}{70}$	
	9.45 A.M.	128	88	78
	9.50 A.M.	100	84	95
	9.55 A.M.	88	83	95
	10.00 A.M.	86	81	
	11.00 A.M.	88	85	
	1.00 P.M.	78	
	2.00 P.M.	78	
	3.00 P.M.	68	

Eight more similar injections were given, with like result, and the patient to the present time prefers this form of treatment to oral administration.

CASE VIII.—J. B., white, male, aged forty years. Coal miner. Auricular fibrillation, with myocarditis. No history of previous infections. Several months previous to admission he experienced shortness of breath, with a fluttering sensation, while at work. He is quite comfortable when at rest. Apex rate 110; $\frac{1}{60}$ strophanthin caused a drop in one hour to 84, the effect lasting for two days.

CASE IX.—M. B., white, aged thirty-six years. Lobar pneumonia, with grave toxemia. Auricular fibrillation, with a heart rate of 160. No dilatation. Two days before his death he received $\frac{1}{60}$ gr. strophanthin, with a drop in heart rate in one hour to 80. The patient's condition remained unimproved, and the heart rate again rose steadily to 150. On the following day he received another injection, with a similar drop, but in spite of this, he became progressively worse, and died the same evening.

CASE X.—A. S., Italian, aged thirty-six years. Lobar pneumonia, with severe toxemia and delirium. Auricular fibrillation, dating back three years. Heart rate, 144. Twenty-four hours before his death, which occurred on his third day in the hospital, he received gr. $\frac{1}{60}$ strophanthin. One hour later the apex beat was 92. His general condition, however, remained unaffected, and with the heart rate rising again steadily, he died the same day.

CASES WITH NORMAL RHYTHM.

CASE I.—R. B., white, female, aged sixteen years. Mitral insufficiency and stenosis. Pulse regular, 100 per minute. Gr. $\frac{1}{120}$ strophanthin caused a drop of eight beats in her pulse rate. It quickly rose again, and by evening the rate was again 100 (Fig. 4).

CASE II.—E. O., female, aged fourteen years. Mitral insufficiency and stenosis, with early decompensation, acute pericarditis, a frail girl; heart, one and one-quarter inches to the right of midline and three and one-half inches to the left in the third interspace. Pulse 120, regular; occasional edema of the ankles; mitral systolic murmur, pericardial frictions. Liver two fingers' breadth below the costal border. Strophanthin $\frac{1}{60}$ gr. produced no effect on the pulse rate. Later she was given tincture of digitalis by mouth, 1 dram a day, until she took 10 drams in all, when it was discontinued, owing to slight headache. The pulse at this time showed occasional slowing, due to a heart-block which had been induced, but which disappeared two days after discontinuing the digitalis.

CASE III.—H. M., aged sixty years. Aortic insufficiency. Pulse 130, regular. Strophanthin $\frac{1}{100}$ gr. reduced the pulse rate from 130 to 125, but within an hour it had risen to the original rate;

it seems scarcely reasonable to interpret so slight a difference as the result of the injection.

CASE IV.—Mrs. C., aged forty-two years. Mitral insufficiency; beginning of decompensation; regular pulse rhythm, 120 per minute. Strophanthin $\frac{1}{60}$ gr. had no effect upon her pulse rate.

CASE V.—C. R., male, aged forty-two years. Mitral insufficiency; pulse rate 110, regular; $\frac{1}{60}$ gr. strophanthin had no effect on his pulse rate.

CASE VI.—Mrs. B., aged thirty-five years. Seen after laparotomy; temperature 22, pulse 120, regular but weak and thready. Strophanthin $\frac{1}{80}$ gr. injected to note any possible effect; the patient was in a serious condition at the time it was given. The injection not only had no effect, but the pulse continued to rise steadily to 180, maintaining its regular rhythm throughout until the time of her death, which occurred the second day.

CASE VII.—B. H., male, aged forty years. Arteriosclerosis; myocarditis; pulse rate, 100. No evidences of decompensation. Dose used $\frac{1}{60}$ gr. There was no lowering of the pulse observed.

CASE VIII.—F. B., male, aged forty-one years. Paroxysmal tachycardia of auricular origin. Myocardial insufficiency. Pulse rate estimated by polygraph, 208 per minute; when seen, the attack had lasted twelve days, coming on without apparent cause in the middle of the night. No history of any previous infections. Skin and mucous membranes moderately cyanotic. Heart apex in the fifth interspace three and a quarter inches from the midline. No murmurs present; liver border, one finger breadth below the costal margin. Strophanthin $\frac{1}{60}$ gr. injected without effect. Edema of the legs came on; the apex of the heart extended out from the midline and the liver gradually went down to the level of the umbilicus. Eleven days after the first injection a second injection of $\frac{1}{60}$ gr. was given at 9.30 P.M. Two hours later no change had been noticed; when next seen, on the following morning, the pulse rate was 84 to the minute and regular. It remained so for the rest of his stay in the hospital. While it is not known at what time the drop in pulse rate began, the patient stated that at midnight following his injection he experienced a sudden relief, and the change in rate probably occurred suddenly at this time.

CASE IX.—A. M., female, aged twenty years. Mitral insufficiency, with advanced decompensation. Had not improved to any extent under oral administrations of digitalis, although she had received in all eight drachms of the tincture. With the onset of nausea, digitalis was discontinued. She continued unimproved and gradually weaker and more dyspneic. Two weeks following the discontinuance of digitalis, and at a time when she appeared to be growing extremely weak, she was given an injection, $\frac{1}{60}$ gr. strophanthin. The pulse rate at the time of giving the strophanthin was 104, and an examination made an hour subsequently showed

that the pulse rate had dropped to 86, but within eight hours it had risen again and death occurred on the same day. Although no records were made with the polygraph, there is little doubt that most of the apparent slowing in this instance was due to the production of extrasystoles.

CASE X.—C. W., colored, aged fourteen years. Endocarditis; pericarditis; acute articular rheumatism. Patient when seen was sitting up in bed, gasping and very weak: pulse rate was regular, and 124 to the minute. It was decided to give her an injection of $\frac{1}{60}$ gr. strophanthin, with the fatal effect observed in the previous discussion.

THE VALUE OF COLONIC INFLATION IN THE DIAGNOSIS OF CHRONIC APPENDICITIS.¹

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THE frequent association of chronic inflammation of the appendix with persistent gastro-intestinal disturbances is being more and more recognized, but the diagnosis of chronic or subacute appendicitis is, nevertheless, a matter of no little difficulty, particularly in those cases which have had no history of a previous acute attack. In many instances, pain in the right iliac fossa, either spontaneous or induced by pressure, furnishes the clue to the diagnosis, but in many other instances there is an absence of this feature, the chief symptom being abdominal pain of more or less definiteness. Granting that there is well-marked pain in the right iliac fossa, one is still not justified in concluding that the cause of the pain is appendicular in origin, without excluding disease of organs situated in the right upper and lower quadrant of the abdomen, notably the Fallopian tube, ovary, kidney, and gall-bladder, a matter at times beset with difficulty.

The frequent occurrence of latent appendicitis and the difficulty attending its diagnosis has led Bastedo to advance a new test, the dilatation test, in order to determine the presence of chronic appendicitis. He passes a colon tube, eleven or twelve inches, into the rectum and injects air by means of an atomizer bulb. "If, as the colon distends, pain and tenderness to finger-point

¹ Read at a meeting of the American Gastro-enterological Society, Atlantic City, June 22 and 23, 1914.

pressure become apparent at McBurney's point there is appendicitis," to use Bastedo's own words.²

The test is not needed in an acute appendicitis and is not required in an undoubted chronic case, but the indication for the method lies in individuals with persistent digestive and abdominal disturbance for which no cause can be found. Also in distinguishing between right-sided pelvic inflammation and an inflamed appendix the test is said to be of assistance. Bastedo concludes his article with the statement: "In the use of the test during the last four years we have had no case in which the test was positive and the operation findings negative. But in two out of all our cases the negative finding of the test was followed within six months by a typical attack of appendicitis, and the test was, therefore, presumably at fault. Several times in the early days of the test surgeons operated for a suspected appendicitis, though the test was negative, and in every such case the appendix was found normal."

Such promise of an easy method of diagnosis has led subsequent observers to study the test, among them being Dreyer,³ Rost,⁴ Slawinski,⁵ and most recently Hertz.⁶ The last-named is particularly enthusiastic and agrees with Bastedo, to wit, that the test is an almost infallible means of diagnosing chronic appendicitis. He warns against its use in cases of acute inflammatory disease of the appendix unless the surgeon is prepared to operate at once, as there is imminent danger of tearing adhesions or causing a diseased appendix to perforate.

Hertz has shown that the only stimulus to visceral pain is distention, but so long as the colon is healthy the pain appears no sooner in the appendix than in the rest of the colon. If there is inflammation of the appendix there is an increased response to the pain stimulus of visceral distention, pain is much more rapidly produced, and as a result, local pain and tenderness are observed in the right iliac fossa. Adhesions do not seem to be the main factor in the production of the pain, as some cases exhibited typical pain without these being present.

Rost⁷ claims that the test is not a specific one for appendicitis, but that the condition of the lower bowel may be similarly recognized by the pain which follows colonic inflation. He quotes, as exemplifying this contention, a case of cecum mobile, which after a fixation of the cecum experienced no pain on inflation, and a case of pain in the left iliac fossa which was shown at operation to be due to chronic adhesions.

Slawinski⁸ has made use of the method for some time and suggests that it be called Bastedo's test.

² AMER. JOUR. MED. SCI., 1911, cxlii, 11.

³ Münch. med. Woch., 1912, p. 1845.

⁴ Ibid., 1912, p. 2055.

⁷ Loc. cit.

⁴ Ibid., 1912, p. 2055.

⁶ Lancet, 1913, i, 816.

⁸ Loc. cit.

The preciseness of the results claimed for colonic inflation has induced us to study the patients admitted to the Presbyterian Hospital during the past year.

The technique employed was as follows: The patient being in a recumbent position, a rectal tube, well greased, is introduced into the rectum for a distance of about three inches. (It is unnecessary to insert the tube as far as eleven or twelve inches as recommended by Bastedo). After the tube has been introduced the patient lies on his back, an atomizer bulb is attached to the free end of the tube, which is brought up between the legs and air is slowly pumped in. In individuals with no appendicular disease there is no pain apart from a feeling of fulness in the lower bowel, with at times a sensation as if defecation was imperative.

In patients suffering from appendicitis it is claimed that there is an almost immediate complaint of spontaneous pain in the right iliac fossa, much exaggerated by finger-point pressure. In those cases of appendicitis with epigastric pain, pain is not complained of in the epigastrium, but in the right iliac fossa, and in cases with pain located in this region the discomfort is intensified. At times pain on pressure over the distended cecum induces pain, not over McBurney's point, but also in the epigastrium as well; this phenomenon being only seen, however, when epigastric pain has been a preëxisting symptom. Aaron⁹ has already described as a sign of chronic appendicitis epigastric pain which follows pressure in the right iliac fossa.

While pursuing our studies it was deemed advisable to examine every patient admitted to the medical ward, provided he complained of no abdominal distress. By doing this we collected about seventy-five cases, presumably normal, so far as the appendix was concerned, and in none was pain complained of in the right iliac fossa following inflation. We feel that this number of cases justifies the belief supported by the experience of Bastedo and of Hertz that normal individuals do not have what may be called positive tests. We therefore discontinued our observations on control cases.

In studying the abdominal cases admitted to the hospital, our work was much facilitated by the ready willingness of the various chiefs of the Presbyterian Hospital, who at all times gladly placed their material at our disposal. We cannot express too strongly our appreciation of the many courtesies extended by Drs. Hodge, Rodman, Jopson, Shoemaker, and Girvin, in whose wards many of the operative cases were observed.

Our results briefly put are not in accordance with those of other writers. There have been in our series of positive tests 3 cases which have had no indication of appendicular lesion; notably 1

⁹ Jour. Amer. Med. Assoc., 1913, lx, 350.

case of cholelithiasis, 1 of nephritis (signs present one day, absent the next; patient later died of uremia), and 1 of right-sided pneumonia, with pain in the right iliac fossa.

Of the negative cases, 7 had appendices chronically inflamed and bound down by adhesions and 5 were suffering with acute appendicitis.

Salpingitis, in our experience, does not give typical pain in the right side. It is true that pain is complained of, but it is low down in the abdomen and not in the region of McBurney's point. We have felt that the sign may have some value in distinguishing between this condition and appendicitis.

CONCLUSIONS. 1. Inflation of the colon is an equivocal means of diagnosing chronic appendicitis. Some cases have negative tests and some have positive; there seems to be no constancy in the result obtained.

2. In acute appendicitis the method should not be employed. It is rarely necessary as a diagnostic aid, as the results are uncertain and the risk of injuring the intestine is too great.

3. The method should not be considered useless, however, for at times the diagnosis has been materially strengthened by its employment, and operation has later shown the wisdom of our faith in the result obtained. Inflation of the colon, however, should be regarded merely as an aid in the diagnosis, history and physical examination being far more valuable.

4. We have seen no positive reactions in normal individuals.

5. The test is in no sense pathognomonic of chronic appendicitis.

DUODENAL ALIMENTATIONS.¹

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PERHAPS the best of the many excellent things which Einhorn has contributed to the science and practice of medicine is the duodenal tube and its practical application to the relief of certain disorders of the alimentary tract. Duodenal alimentation has been practised during the past four years by an increasing number of medical men throughout the United States, Canada, and Europe, and wherever it has been intelligently carried out it has gained a permanent place in the treatment of suitable cases. Whenever duodenal alimentation has failed it has been due, in my opinion,

¹ Read by invitation before the Pittsburgh College of Physicians, February 26, 1914.

to one of two causes, which have ever in the past operated to bring into temporary discredit many excellent methods of instrumentation, namely, inappropriate application or faulty technique.

The demands which duodenal alimentation satisfy and which give it the right to a permanent place in medical means and measures are the almost complete rest of the stomach, with lessened activity of the duodenum, and the supplying of sufficient calories for maintaining the individual's nitrogen balance and body weight. No other method, except feeding into the stomach itself, is capable of sustaining life for more than short periods of time. I have often fed patients continuously and exclusively for four weeks by this method, and in one instance the patient was so fed for five weeks without during this period, once removing the tube, and with a gain of five pounds in weight. This patient had had recurrent symptoms of duodenal ulcer during several years previously, and had been treated with more or less temporary benefit in several of the large cities of Europe before coming to America. She had had, now and then, quite pronounced hemorrhages from the bowel, accompanied by some symptoms of collapse. Her other symptoms were also more or less typical. After the removal of the duodenal tube she quite rapidly resumed her normal diet and accustomed round of duties, and has remained in good health during the two years which have elapsed since the termination of the treatment.

This case is only one from a large number of similar cases, and is cited to answer two oft-repeated questions, to wit: whether this method is suitable in duodenal ulcer cases, and whether there is danger in leaving the tube *in situ* over long periods of time.

The principal field of usefulness for duodenal feeding is in the treatment of gastric and duodenal ulcers, but it may be and is used with equal benefit in pylorospasm from any cause, provided the bucket can be gotten through the pylorus. The relief from pain afforded some of these patients is almost as marked as that afforded by hypodermic medication.

There is another class of very trying cases in which this method of feeding acts most happily—namely, gastropnoia and gastrectasis with or without isochymia, in which, owing to the low position of the stomach or to atony of its musculature, the stomach is incapable of propelling the food on into the duodenum with sufficient rapidity to supply the body needs. These patients rarely fail to respond promptly to duodenal feeding if properly carried out.

I am treating duodenal catarrh by inserting the duodenal tube, and after washing the mucosa with water I allow 500 c.c. of a 1 to 500 solution of argyrol to flow in more or less rapidly so as to distend the gut. Two or three such treatments repeated at intervals of three or four days rarely fail to relieve these patients.

In several cases of inoperable cancer of either the cardia or the pylorus, accompanied by increased pain during and after meals,

I have been able to pass the tube into the bowel and institute duodenal feeding, with marked relief, for some time. In such cases we must be careful not to leave the tube *in situ* until the stenosis reaches a degree where it becomes impossible to withdraw it on account of the size of the gold bulb.

Another class of cases in which duodenal feeding may often prove of benefit is the severe vomiting of pregnancy. This method should at least be tried before resorting to more extreme measures. The only difference in applying this treatment in these cases is that the duodenal tube should be somewhat longer and so be introduced far down in the jejunum. I have tried this in only one case, and it proved successful to the extent that we were able to tide the patient along until the fetus was viable, thus enabling the mother to give birth to a living child.

Einhorn is using duodenal feeding in cirrhosis of the liver and has noted some striking results therefrom, a report of which he gave in an excellent paper which he read before the sixteenth annual meeting of the American Gastro-enterological Association. I quote the summary with which Einhorn closed his paper: "During duodenal alimentation in all the six patients the liver became markedly smaller (already after two or three days), assuming a size almost normal. In four patients the result was lasting. In one, however, a few days after the termination of feeding the liver began to grow larger, while in another patient with pure cirrhosis and dilated heart the size of the liver quickly assumed its original large proportions. The influence of duodenal feeding was in this case very marked but not lasting.

"My experience thus far justifies me in the conclusion that duodenal alimentation contributes greatly toward diminution of the functional work of the liver. This rest treatment for the latter organ is of benefit, whenever it is considerably impaired. The cirrhosis of the liver and allied conditions accompanied principally by swelling of the hepatic tissues form a field in which duodenal alimentation may be applied apparently to a great advantage."

In idiopathic hyperchlorhydria, which resists all other measures, duodenal feeding usually affords relief by reducing the hypersensitiveness of the gastric mucosa. In these cases the treatment should be prolonged for three or four weeks to secure permanent results.

Another important use I have made of the duodenal tube is in the treatment of amebic dysentery. For a long time ipecacuanha has been recognized as the most powerful medicament in the treatment of amebic dysentery. It has, however, always been difficult to administer this drug in sufficient amounts to effect a cure on account of its emetic action. By introducing the tube well down into the gut and forcing an emulsion of ipecacuanha through it a sufficient dosage may be administered to check the action of the

ameba coli in the gut, and thus in some cases cure the disease. It is often necessary to repeat the dose several times at intervals covering a period of several weeks to finally control the disease. Rarely, if ever, has vomiting been induced by the ipecacuanha when given through the duodenal tube. It is necessary to prepare the patient for this treatment by giving a sharp purge the day before and limiting the food to liquids. After administering the ipecacuanha it is wise to have the patient remain in bed for the ensuing twenty-four hours. After considerable experience with this method, and with emetin given hypodermically, I feel that perhaps the duodenal tube method is as reliable as the hypodermic method, and the duration of treatment is likely to be shorter. Another point in favor of the duodenal tube is that the patient can readily be taught to give it to himself should the case prove stubborn, necessitating several repetitions of the procedure.

In the light of maturer experience in the treatment of amebic dysentery by emetin which Dr. Vedder, of the United States Army, has had, the results of which are set forth in his splendid article,² the following conclusions may be drawn: Emetin has the power to kill the vegetable ameba in the tissues, but has no effect on the entameba hystolytica, since they still persist in the stools of individuals who have had a thorough course of treatment with emetin; whereas the ipecacuanha given through the duodenal tube destroys the entameba hystolytica in the intestinal tract, but has very little effect on the ameba in the tissues. Therefore, it would seem that the best results might be secured by the use of the combined methods, to wit: giving the emetin hypodermically in small daily doses and giving the ipecacuanha through the duodenal tube once or twice a week for several doses.

As I have already mentioned the fundamental indication calling for the use of the duodenal tube is rest for the stomach and duodenum. Therefore all those bodily conditions which are benefited by putting this part of the alimentary tract in splints call for this method of treatment. The second indication for the use of the duodenal tube is for the administration of foods or medicine in such amounts as would otherwise be rejected by the stomach. The third indication is to secure duodenal contents for examination to aid in diagnosing certain disorders of the digestive system beyond the stomach.

As to the limits of usefulness of duodenal alimentations, it may briefly be said that they will be determined by the dictates of the rules which apply to other methods used in such cases.

Contra-indications to the use of duodenal tube are few: for instance those cases where the degree of stenosis is such that the bulb does not readily pass the obstruction, and in those rare cases

² Jour. Amer. Med. Assoc., February 14, 1914,

where there is such hypersensitiveness of the mucosa of the throat as to induce constant retching and pain. Now and then we find an individual whose duodenal mucosa is so hypersensitive that each feeding causes purging regardless of the kind of food administered. Happily these cases are rarely met.

In those cases where the pylorospasm, from whatever cause, has persisted so long as to impair the patient's general health to a degree demanding immediate relief of the stenosis, we should advise operative interference.

In this connection I wish to say that moderate hemorrhage from the esophagus, the stomach, or the duodenum is no contra-indication to the employment of the duodenal tube.

Einhorn's apparatus consists of a small gold bucket perforated by several small openings, and capable of being taken apart for the purpose of cleaning: a rubber tube of small caliber leading to the bucket; a rubber pet-cock and a feeding table, an ingenious arrangement which rests over the glass of nourishment so that the food may be drawn up through one tube into a glass syringe, and by manipulation of the pet-cocks be forced slowly into the tube connecting with the duodenal tube, without disconnecting the syringe.

The technique is as follows: At night the patient with the aid of water swallows the duodenal tube. During the night the bucket will usually pass into the duodenum. I have found it is well to give one-half grain of codein one hour before the tube is introduced, to allay the spasm of the throat and to insure a quiet night's rest. The second line on the tube is supposed to be at the incisor teeth, the bucket is at the pylorus, and when the third mark has reached the teeth the end of the tube is probably *in situ*, well down in the duodenum. When this is accomplished the tube is allowed to remain in place during the entire course of treatment. During the first twenty-four hours some of the patients have been somewhat uncomfortable from sore throat, due to the presence of the tube in the throat; but this has never been severe enough to occasion the withdrawal of the tube on this account, and usually in from twenty-four to forty-eight hours they have become accustomed to it and do not mind it.

How can we tell that the tube is through the pylorus? By slight traction a resistance is felt if the tube is in the duodenum; aspirations through the tube with a glass syringe bring typical, golden-yellow, duodenal juice of neutral or feebly alkaline reaction and not acid gastric juice; lastly, if the patient is given a glassful of milk and water to drink, and if aspiration is immediately performed, the milky solution will not be returned through the tube if the end is in the duodenum, as it would were it still in the stomach.

The feedings are given at two-hour intervals during the day. The food which has been most satisfactory is a mixture of milk,

raw eggs, and sugar of milk. Not infrequently individuals are met in whom eggs are not tolerated; in these patients eggs produce distress after the feeding, and if persisted in give symptoms of acute ptomain poisoning. The amount of food which should be given at a feeding is from 150 c.c. to 300 c.c. of milk, one raw egg, and 15 gm. of sugar of milk. It is wise, however, to begin with smaller quantities, 100 c.c., and work up to the full amount as soon as possible.

It is important that the feedings simulate nature's method as nearly as possible, and to this end the food must be heated and strained and then given slowly through the tube. Under ordinary circumstances the stomach performs, among its other duties, the function of withholding food from the duodenum until of a correct temperature. Too hot foods are cooled and cold foods are not propelled from the stomach until they are warmed to the body temperature. It is important to bear this in mind in undertaking duodenal feeding, as the duodenum is most sensitive to variations in temperature, reacting to each shock, as well as to too rapid administration of food, by causing a feeling of nausea, discomfort, restlessness, clammy perspiration, etc. After each feeding the duodenal tube must be carefully cleaned by forcing a syringe of water through it, followed by a syringe of air, after which the pet-cock is closed before the syringe is disconnected. Failure to keep the tube clean will result in its becoming entirely blocked by a tough coagulum of milk and egg, which will necessitate frequent and annoying withdrawal of the tube.

As previously reported, the first two cases which I treated by the duodenal method of feeding were unable to take a sufficient quantity of nourishment at a feeding without producing untoward symptoms of nausea and distress, and therefore I modified the method in the following manner: Instead of the syringe I make use of the gravity and drop method, as in giving salt solution by the Murphy method. The duodenal tube is connected to a tube leading from a pint irrigating jar, and the flow regulated so that the 300 c.c. used at a feeding takes about twenty-five minutes to pass through. The milk may be kept warm by having the conducting tube pass through hot water or under a hot-water bag, etc.

During the period of duodenal feeding, in order to increase the amount of fluids supplied to the body, normal salt solution may be given every day by the drop method through the rectum.

CASE I.—Aaron S., aged forty-nine years; night watchman. Family history negative. No history of venereal disease. Healthy up to six years ago, when the symptoms for which he later came to me made their appearance. At that time a diagnosis of biliary colic was made by another physician and the gall-bladder was opened and drained. No gall-stones or other disease was found. Later on, the symptoms still persisting, appendectomy was done,

with no relief. He first came to me in the early part of January, complaining of burning pain in the stomach, coming on three or four hours after meals, and which was relieved by the taking of food or alkalies. He had also acid regurgitation. The physical examination was negative except for a spot of tenderness on pressure over the lower right-hand quadrant of the epigastrium. The thread test was positive for gastric ulcer, showing a blood-stain 50 cm. from the incisors. The *x*-ray report was as follows: "There is a deformity of the duodenal cap which is probably spasmodic in origin. A six-hour residue, which is due to pylorospasm. These findings are confirmatory of ulcer of the stomach."



FIG. 1.—Case I. Mr. A. S.

On January 15 the patient was put upon duodenal feeding, which was maintained continuously for eighteen days. At the end of the first twenty-four hours all the gastric symptoms had disappeared; a few days after the withdrawal of the tube he was able to resume a practically normal diet, excluding only the more irritating articles of food. At the present time he is entirely free from symptoms.

CASE II.—Herbert H., aged twenty-five years; single; private secretary. Family history negative. No venereal history. Had an attack of jaundice six years ago lasting one month. When he came under my observation he had been suffering for two months from an acute severe pain beneath the inner half of the right costal border, which extended through to the right scapula, coming on about two hours after lunch. The chest organs were normal, so also were the liver and kidneys. There was a tender point on

pressure beneath the inner half of the right costal arch. The thread test was positive for duodenal ulcer, showing a stain 57 cm. from the incisors. The x-ray report was as follows:

"The absence of a well-defined cap in three sets of radiograms and the rapid emptying of the stomach are confirmatory of duodenal ulcer." The patient was put on duodenal feeding for two weeks, at the end of which time all symptoms had disappeared. Two weeks after the withdrawal of the tube he was eating a liberal, though soft diet, and has remained well.



FIG. 2.—Case II. Mr. H. R. P.

CASE III.—Timothy T. A., aged forty-one years; married; Congressman. Family and venereal history negative. Had been healthy up to nine years ago. During the past seven years had had increasing digestive disorders. In August, 1912, had severe hemorrhage from the bowels, at which time a diagnosis of duodenal ulcer was made, for which he was operated upon. The diagnosis was confirmed at the operation. The ulcer was not excised, but a purse-string suture was used and the ulcer turned in.

He came to me the following January with a history of having passed blood from the bowel almost daily since the operation. He was pale, almost chalky. The conjunctivæ and lips were bloodless. The hemoglobin was 33 per cent.; red-blood cells, 3,000,000; leukocytes, 5200. The chest organs were normal, so also were the liver and kidneys. Examination of the feces showed them to contain a large percentage of coagulated blood. The thread test was positive for duodenal ulcer, showing a blood

stain 68 cm. from the incisor teeth. No x-ray examination was made in this case, as the diagnosis was so obvious and immediate treatment urgent. He was put at once upon duodenal alimentation, and within five days the macroscopic blood had disappeared from the stool, and within three weeks the feces were negative for occult blood, and have remained negative since that time. The tube was left *in situ* for twenty-eight days. On withdrawing it his diet was gradually increased to solid but bland foods, on which he remained until the latter part of the summer, since which time he has been eating his normal diet. The condition of the blood gradually improved until it is practically normal, the hemoglobin being now 81 per cent.



FIG. 3.—Case III. Mr. T. T. A.

In a former paper I called attention to an interesting case of tic douloureux, which appeared to be almost entirely cured by a course of duodenal alimentation. In this case the patient had already previously determined that there was a distinct connection between her attacks and the condition of her stomach. She could often foretell the appearance of an attack. This case proved to be one of extreme gastropptosis with gastrectasis, and with a marked degree of hyperacidity of the gastric juice. Duodenal alimentation was carried out for four weeks and brought about an almost complete cure. During the years which have elapsed since that treatment the patient has suffered only momentary "jabs" of pain in the affected area, and these occurred only after some dietetic indiscretion. It is interesting in this connection to note that the lower

border of her stomach has gradually come up from the upper border of the symphysis pubis to practically the normal position. This result may be expected in a large majority of cases of gastrectasis, provided a suitable line of treatment is carried out in addition to the duodenal feeding.

The cases cited above are merely to illustrate what may be accomplished with duodenal alimentation.

TUBERCULOSIS OF THE BRONCHIAL GLANDS AND LUNG HILUS: A CLINICAL AND RADIOGRAPHIC STUDY.¹

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AND

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FREQUENCY OF THE CONDITION. By whatsoever route tubercle bacilli enter the body, be it through the alveolar wall, the bronchial mucous membrane, or by way of the gastro-intestinal tract, they ultimately reach the bronchial glands in the great majority of instances.

In a series of 569 cases of tuberculosis, Comby² found the bronchial glands involved in all, and Hamburger and Sluka observed a like condition in 110 cases. Haushalter and Frulinsholz³ found the bronchial glands tuberculous in 74 out of 78 infants dying of acute tuberculosis, or tuberculous meningitis.

As commonly used, the term bronchial glands includes the glands at the sides of the trachea and the group just below its bifurcation, as well as the glands surrounding the bronchi.

The largest ones are usually found below the right bronchus. The tracheal group are in relation to the superior vena cava and the vagus and recurrent laryngeal nerves. Owing to the lower origin of the left recurrent nerve, it is in contact with the trachea for a longer distance than the right one, and more often shows the effect of pressure by paralysis of the left vocal cord. When the glands attain a large size, they may press upon the arch of the aorta and its branches, the innominate veins, and the phrenic nerves.

The pericardium is anterior to the infratracheal group, and the

¹ Read before the Hartford Medical Society, June 15, 1914.

² Quoted by Grenet, *Anal. d. Méd. et Chirg. Infant.* Paris, 1911, xv, 497.

³ *Archiv. d. Méd. d. Enfant*, 1902; quoted by Grenet, *op. cit.*

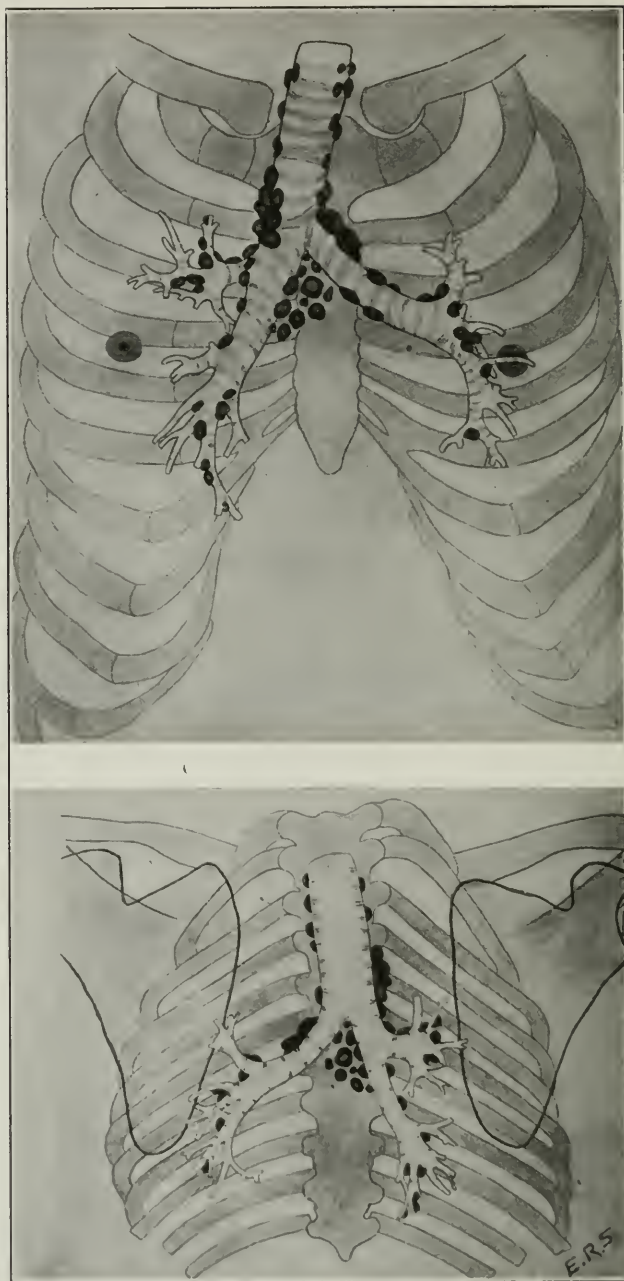


FIG. 1.—Composite drawings showing the relationship of the bronchial glands to the thoracic wall in the adult. The glands are according to Sukiennikow (*Berl. klin. Woch.*, 1903, xi, 316, 347, 369) and the trachea and bronchi are after Blake (*AMER. JOURN. MED. SCI.*, 1899, cxvii, 320). In the child the trachea bifurcates at about the level of the intervertebral disk between the fourth and fifth thoracic vertebrae, which corresponds nearly to the tip of the fourth thoracic spine. This is about opposite the articulation of the third costal cartilage anteriorly.

esophagus is behind and slightly to the left. The vagus nerve is also in relation to this group. The hilus glands are in contact with the lung and the bronchial and pulmonary vessels. The location of the several groups is shown in Fig. 1.

Leroux⁴ has stated that the glandular lesion is usually unilateral from the second to the fifth year, but that after that period it is more apt to be bilateral. Harbitz⁵ found the oldest lesion more often in either the hilus, infratracheal and peritracheal groups than in the bronchial glands proper. Up to the fifteenth year the glandular form of tuberculosis predominates, but after that age the pulmonary form is more common.

Just how the infection of the lung is brought about we do not know, though much experimental work has been done. The belief has been quite general that the bacilli after penetrating the alveolar wall or bronchial mucous membrane are promptly borne by the lymphatics to the bronchial glands. Here they may remain until the lymphatics, becoming obstructed and dilated, reverse their flow and the tuberculous lymph backs up into the lung. As early as 1876 Parrot⁶ opposed this theory. He stated that he was always able to find a lesion in the lung that was older than the glandular one, though a diligent search might be required to discover it, as it was not infrequently very small. So constant were his results that he taught his pupils that the bronchial glands were "the mirrors of the lungs."

Others have since confirmed his results, and Ghon⁷ has reported finding a primary lung lesion in 92 per cent. of 184 cases. The lesion was frequently small and often single. Ghon considers the latter fact good evidence against the theory of infection from a reversal of the lymph current. Inasmuch as it is commonly taught to search the apices for the earliest sign of tuberculous disease it is especially noteworthy that the primary focus was more often found in the lower lobe than in the upper.

Shika⁸ has recently stated that in six years of x -ray work, devoted wholly to children, he found only three cases of apical tuberculosis.

Harbitz,⁹ studying the modes of dissemination of tuberculosis in children, found that the lungs were commonly infected through the rupture of a caseous gland into a bronchus, usually near the hilus. This resulted in a caseous bronchopneumonia in the distribution of this bronchus.

By the use of the x -rays, Sluka¹⁰ found that the hilus of the lung,

⁴ Archiv. d. Méd. d. Enfant, 1908; quoted by Grenet, op. cit.

⁵ Jour. Infect. Dis., 1905, ii, 143.

⁶ Mémoires d. l. Soc. de Biol., 1876, p. 308.

⁷ Der primäre Lungenherd bei der Tuberkulose der Kinder, Berlin, 1912 (Ed. Jour. Amer. Med. Assoc., 1912, lix, 1544).

⁸ Wien klin. Woch., 1914, xxvii, 173. Abs. AMER. JOUR. MED. SCI., 1914, cxlvii, 770.

⁹ Loc. cit.

¹⁰ Wien. klin. Woch., 1910, xxiii, 156.

as well as the glands, was always involved in young infants, and frequently in older children as well.

SYMPTOMS. We do not know how long after infection takes place before symptoms and physical signs develop. Straub¹¹ is of the opinion that the primary lung focus is not accompanied by symptoms, and that they do not appear until the bronchial glands and adjacent lung becomes involved. Usually the onset is insidious, and the symptoms, which are those of a toxemia, are suggestive rather than conclusive, but their vagueness should awaken our suspicion. They often start from childhood, frequently developing after whooping cough or measles. A sense of weariness is usually present, and if the patient be a child, inquiry will show that he does not romp and play with the other children, but listlessly "sits around." The appetite is usually capricious, and the child is often irritable. Sometimes complaint is made of a sharp pain within the chest, which may radiate to the shoulder. Again, an interscapular backache may be almost constant. Vague digestive disturbances may predominate the scene, suggesting a mild form of muscular insufficiency. Phillippi¹² found hyperchlorhydria rather common. Persistence of these symptoms in a young adult who is below weight calls for investigation of the lung hilus region, as the apical signs may be equivocal or absent. The temperature is often subnormal, especially in the morning, though an afternoon rise is usually present. Occasionally the cheek on the side of the lesion will flush with every little excitement; rarely are the pupils unequal.

Often, perhaps usually, the patient has a cough; when brassy and "explosive" in quality it is extremely suggestive of bronchial adenopathy. These children "catch cold" easily, and with each cold the already swollen lymph nodes become somewhat larger, and pressing on the vagus a cough develops. The cough not infrequently causes gagging, and sometimes even vomiting occurs. But it should be much more generally appreciated that cough may be insignificant, and even entirely absent, as it was in the child whose radiograph is here shown (Fig. 7). Night sweats seem to be the exception, rather than the rule.

It has been found that infants with tuberculosis of the bronchial glands are prone to attacks of dyspnea, in which the stridor is chiefly or wholly expiratory in character, thus differing from thymic asthma, in which the dyspnea is inspiratory. As the disease progresses, the dyspnea affects both inspiration and expiration. In a number of instances the condition has been mistaken for one of laryngeal diphtheria, and intubation has been performed, but without relief. The persistence of the voice in bronchial aden-

¹¹ *Beit. z. Klinik. d. Tuberk.*, 1912, xxiv, 283.

¹² *Ibid.*, 1911, xxi, 67.

opathy and its absence in diphtheria should make this mistake infrequent.

In Guisez's case,¹³ where the dyspnea was mechanical from glandular pressure, passage of the bronchoscope brought instant relief.

Very alarming symptoms may arise from the rupture of a caseous gland into the trachea or a bronchus. The child in apparently good health is suddenly seized with extreme dyspnea and death may occur before assistance can be obtained. Goodman¹⁴ has recently collected from the literature a number of such cases. Some years ago Hall¹⁵ reported the recovery of a patient after coughing up a caseous gland which had ruptured into his bronchus. Perforation of the esophagus has also occurred, and death has immediately followed the erosion of one of the large bloodvessels (Fisher,¹⁶ Barry¹⁷).

There is nothing more puzzling to the physician than the patient who spits blood, but has no sign of a pulmonary lesion. It is probable that in some cases the blood comes from the rupture of a vessel in the mucous membrane of a bronchus overlying a tubercle, possibly the primary focus. In other cases, coughing causes a rupture of a bloodvessel already distended from the pressure of enlarged bronchial glands (Griffin,¹⁸ Barthez and Rilliet¹⁹).

A few years ago we had as a patient a boy who had a number of profuse hemorrhages. Repeated examination disclosed only signs of bronchial adenopathy—increased whisper interscapularly (D'Espine sign). We have recently been informed that he has developed well-marked signs of pulmonary involvement.

PHYSICAL SIGNS. *Inspection.* While peribronchial tuberculosis can often be recognized in the adult, it is more common in children, and the signs are usually more marked in early life. The child is usually, but not always, frail. Some years ago, one of us (Stoll) found, by means of the von Pirquet tuberculin test, that the delicate child was about four times as apt to be tuberculous as his more robust playmate.

Dilated veins interweaving across the chest usually indicate glandular pressure, though in one case where they were particularly marked, both physical signs and the x-rays were negative. Expansion may be diminished at one apex, which will be seen to "lag" with inspiration. If the breath be held at the end of inspiration and one observes the hilus region (anteriorly comprising that part of the upper two interspaces between the midclavicular and parasternal lines), an apparent retraction will frequently be noted

¹³ Bull. Soc. d. Pediat. de Paris, 1911, No. 3, p. 114.

¹⁴ Jour. Amer. Med. Assoc., 1913, lxi, 1442.

¹⁵ AMER. JOUR. MED. SCI., 1899, cxvii, 185.

¹⁶ Lancet, London, 1909, i, 28.

¹⁷ Med. Rec., New York, 1891, xxxix, 166.

¹⁸ Quoted by Coley, A Practical Treatise on the Diseases of Children, 1816, p. 185.

¹⁷ Med. News, 1885, xlvii, 236.

on one or both sides (Figs. 2, 3, 4, and 5). Usually this is only a simulated retraction, and is occasioned by the failure of this particular part of the chest to expand. This "dimpling" of the hilus region with inspiration is best seen when the patient is seated in a slanting light from a side window. The patient should be turned from side to side, as an oblique light brings out the depression best. The maximum depression is usually in the second interspace. In patients with hilus disease of long standing, when cicatrization has taken place, a well-marked depression is constantly present. Only rarely have we found the sternomastoid muscle of the affected side in spasm. In a few instances the intercostal

FIG. 2

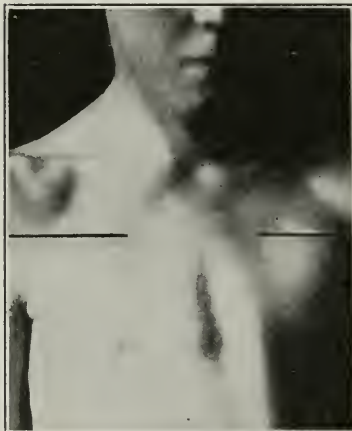


FIG. 2.—R. P., aged fourteen years. Bilateral hilus disease of several years' duration. Aortic second accentuated and "cog-wheel" breathing, with harsh inspiration over left hilus. Posteriorly slight paravertebral dullness and d'Espine's to the fifth thoracic spine.

FIG. 3



FIG. 3.—R. H., aged fourteen years. Bilateral "hilus dimple" and whispered voice over the sternum to the fourth cartilage. Bilateral paravertebral dullness and very marked d'Espine's to eighth thoracic spine. The x-ray picture shows a "well-marked shadow to the right of the vertebral column, above the cardiac shadow (paratracheal glands).

muscles over the hilus region showed some rigidity, but we have not been able to feel the confidence in this sign that Pottinger²⁰ does. Noeggrath²¹ was able to demonstrate Head's zones—areas of superficial tenderness—in the majority of the children examined who were suspected of having tuberculosis. The areas involved were those supplied by the second, third, and fourth thoracic and the fourth cervical, which suggests disease of the base of the lungs and the bronchial glands.

²⁰ Jour. Amer. Med. Assoc., 1909, lli, 771; also AMER. JOUR. MED. SCI., 1909, cxxxvii, 669.

²¹ Jahrb. f. Kinder., 1911, xxiv, 74; reviewed by Michael, Amer. Jour. Dis. Child., 1912, iii, 186

Firm pressure over the sternoclavicular articulation and over the midthoracic vertebral spines may elicit pain. This is only present when the disease is active.

FIG. 4



FIG. 4.—H. B., aged fourteen years. Dilated veins, slight dulness, and bilateral "hilus dimple." Rales . . . Posteriorly, whispered bronchophony heard throughout the interscapular space. For the X-ray findings see Fig. 8.

FIG. 5



FIG. 5.—L. H., aged fifteen years. Bilateral "hilus dimple" and slight retraction below right clavicle. Inspiration cog-wheel and in the first two spaces on the left very harsh. The intercostal muscles overlying were in slight spasm, as was the sternomastoid of that side. Aortic second was accentuated and the whispered voice was present over the whole of the sternum and throughout the interscapular space. For x-ray see Fig. 10. Her history as given by her mother is quite typical. "Never robust; always 'ailing,' subject to colds with cough; often sore throats; strength and appetite poor. Is irritable and indisposed to play. Recently pain across the chest."

Percussion. Percussion, if sufficiently delicate, is a valuable diagnostic measure, but as usually performed so much normal lung is set into vibration that the dull note from the diseased focus is completely lost. In a former paper²² this is discussed at length. Both a light and very light stroke should be employed, the latter being only a tapping with the middle finger of the right

²²Amer. Jour. Dis. Child., 1912, iv, 333.

hand upon one of the terminal phalanges of the left hand, which is held firmly against the chest. It is as important that the finger be held firmly against the chest wall as it is that the blow should be a light one. Ewart²³ has happily referred to this very light percussion as "the percussion of the deaf," which means that the "feel" is as significant, perhaps, as the note obtained.

Dulness from the bronchial glands is sometimes met with anteriorly in the upper two interspaces in the parasternal line, more often on the right side. One should be familiar, however, with the slight degree of dulness normally present in the first interspace to the right of the sternum. A dull note over the sternum is rarely due to enlarged bronchial glands, but may be caused by enlargement of the glands of the anterior mediastinum. In children it is usually caused by an enlarged thymus, and, as a rule, extends to the left in the first interspace for a centimeter or more.

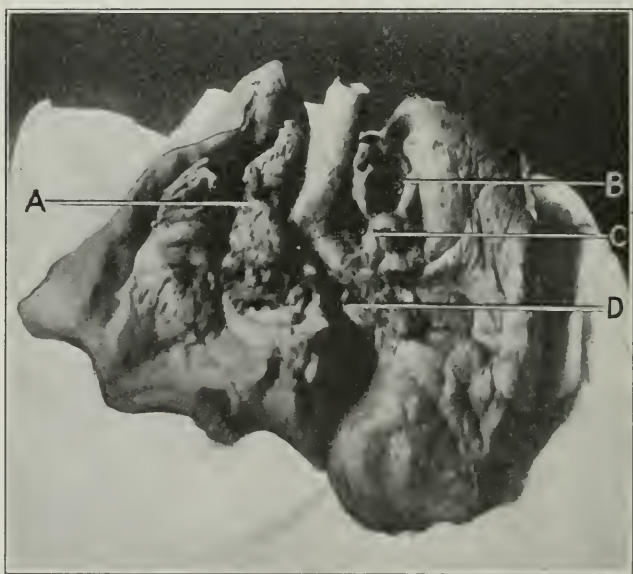


FIG. 6.—Enlarged bronchial glands in the case of H., who had had a marked d'Espine's sign for several years. An anterior view, the heart having been removed. A, large group of glands to the right of the trachea and above the right bronchus; B, cross-section of aortic arch; enlarged glands; C, above left bronchus; D, under left bronchus. The intratracheal group not enlarged.

Percussion posteriorly is usually more valuable than anteriorly. Ewart, long a champion of percussion of the spinous processes, has recently become an advocate of paravertebral percussion, which Kramer,²⁴ Nagel,²⁵ and others consider much superior to percussion of the spinous process.

²³ Prog. Med., 1913, xv, 68.

²⁴ Beil. z. klin. d. Tuberk., 1909, xiv, 335.

²⁵ Jahrb. f. Kinderheil., 1908, 68, 46.

The relation of the hilus to the posterior chest wall is shown in Fig. 1. It is somewhat higher in children than in adults. Bing²⁶ has described a normal hilus dulness of limited extent, which is more pronounced on the right. More recently, Ewart²⁷ has drawn attention to the fact that the area of normal hilus dulness changes with respiration, being wider with expiration and narrowing at the end of the full inspiration. A "suppression of the inspiratory oscillation" on one side he considers indicative of a pathological process of that side.

As the outer border of dulness is usually the most difficult to determine, it seems to be of more practical value to observe the differences in the note at the sides of the vertebræ at the extremes of the respiratory act rather than to depend upon the differences in size of the dull area, though this is sometimes evident. As a rule, we have not been able to feel sure of the "normal hilus dulness" in healthy children, when percussing during quiet respiration.

It does not seem that very slight dulness in this region is sufficient evidence of enlarged bronchial glands, unless accompanied by other signs. Nor does the absence of dulness exclude glandular enlargement. For posterior percussion, a patient should be seated on a stool, with arms well crossed over the chest. The head is slightly inclined forward, and the upper and inner border of the lungs is outlined by König's method. The normal curve of the inner border reaches the vertebral column between the second and third thoracic vertebræ. With enlarged tracheal glands this border is often displaced outward. A dermatographic pencil is used, and one should verify his findings with closed eyes. Dulness is most commonly met with at the sides of the fourth and fifth thoracic vertebra, and more often on the right than on the left. It seems probable that the glands are not alone concerned in this dulness. The engorgement of the bloodvessels and lymphatics, which exists in the hilus region during the acute stage, is in all probability an important factor. The unsuccessful attempt to locate a golf ball in a loaf of bread by percussion strengthens this opinion. The increase of dulness noted at the end of expiration is in part due to the diminution in the air content of the lung and also to the increased congestion which Sewall and Childs²⁸ have shown attends that period of respiration. Direct percussion of the vertebral spines has not proved as satisfactory as paravertebral percussion. With a large mediastinal tumor a dull note may be obtained over the fifth and sixth thoracic spines.

Auscultation. Grancher²⁹ maintained that a diminution of the respiratory murmur was an early sign of enlarged mediastinal glands. We have met with this but twice. Once in a woman with

²⁶ Ugesk. f. Laeger, 1910, lxxii, 199.

²⁷ Loc. cit.

²⁸ Archiv. Int. Med., 1912, x, 45.

²⁹ Bull. acad. de Méd., 1906, lxx, No. 35; abstract Jour. Amer. Med. Assoc., 1906, xlvii, 2011

advanced Hodgkin's disease, and the other time in the child whose x-ray is here shown (Fig. 7).



FIG. 7.—H. A., aged ten years. Referred by Dr. W. G. Murphy. There was slight dullness in the two right interspaces near the sternum. Very dull in the third space, extending to the parasternal line. Respiratory sounds much diminished over right lower lobe. A few rales in inner third first interspace and over lower lobe. Posteriorly no paravertebral dullness but d'Espine's sign, more marked on the left than on the right, was heard as low as the inferior angle of the scapula. Aortic second sound accentuated. The x-rays show extensive disease of the right hilus. The inner end of line *C* indicates the right border of the heart. The left border of the trachea is indicated by *A*. Line *B* shows the beginning of the left bronchus. Notwithstanding this extensive lesion this child had no cough. A footnote refers to the autopsy findings in this case.

A harsh inspiration, often "cog-wheel" in type, was sometimes heard over the hilus region anteriorly. The x-rays showed hilus disease of the side where this type of breathing was noted in several cases, and we are inclined to think this may be a valuable sign of hilus involvement. In one instance the x-rays showed bilateral hilus disease, and the harsh inspiration was noted only on one side. In this case there was spasm of the intercostal muscle over the area of harsh inspiration, suggesting that this was the more active lesion. In one patient the breathing was quite bronchial near the spine of the left scapula.

In a considerable number of children with signs of enlarged bronchial glands, one may detect fine crepitations in the vicinity of the nipple. They may be apparent only on coughing, and are not to be confused with atelectatic rales, which disappear after one or two deep breaths. Miller and Woodruff³⁰ found that the children with these rales gave a much higher percentage of positive reaction to tuberculin than other children.

³⁰ Jour. Amer. Med. Assoc., 1909, lii, 1016.

Several times an accentuation of the aortic second sound has been noted, and in one such case coming to autopsy there was a group of enlarged glands between the aorta and the chest wall.

Of particular importance is the character and distribution of the voice and especially the whispered voice. In the normal individual if the stethoscope be pressed firmly against the chest wall, the area of transmission of the whispered voice is slight. Anteriorly it is normally heard throughout the first right interspace, and in the inner half of the left, and posteriorly it is not present below the seventh cervical spine in children and the fourth thoracic in adults.

There is a peculiar quality to the whispered voice that is of the greatest significance. It consists in a continuation of the sound for a moment after phonation has ceased. It is best brought out by having the patient whisper "three thirty-three" (children can usually say "tree, tree, tree" more easily), when it will be observed that the final "e" of the last word "three" has an echoing quality and persists a moment after speech has ceased. This postphonal element alone is significant. For many years, D'Espine³¹ has diagnosed enlargement of the bronchial glands by this sign alone. He observed that in children the tracheal quality of the whispered voice did not normally extend below the seventh cervical spine. When heard over the upper thoracic vertebræ, he considered it indicative of bronchial adenopathy. It is usually heard for a variable distance at one or both sides of the vertebræ, and to be of significance in adults it should extend at least as low as the fifth thoracic. The diagnostic import increases with the area of distribution.

Sewall³² attributes the whispered bronchophony to congestion of the lung parenchyma, and he considers it the earliest evidence of tuberculous infiltration. In a few of our cases, where stereoradiographs were taken, the fine lines were seen to extend to the surface of the lung in the interscapular region, which would seem to support Sewall's theory. From the result of the autopsy findings in four of our cases, however, we are inclined to think that the glands lying along the trachea and bronchi play a large part in the transmission of the tracheal quality to the whispered voice.

The intensity of the bronchophony, moreover, is usually much increased by flexing the head well forward, which carries the trachea and bronchi with their glands backward toward the vertebral column.

This sign was well marked in three out of four adults in the Hartford Hospital, with aneurysm of the aortic arch, presumably from pressure on the left bronchus. Both Zabel³³ and Koch³⁴ have

³¹ Bull. Acad. de Méd., 1907, lvii, 167.

³² Loc. cit.

³³ Münch. med. Woch., 1912, lix, No. 49; Jour. Amer. Med. Assoc., Abs. 1913, lx, 250.

³⁴ Tribune Med., 1912, viii, 381; quoted by Da Costa, AMER. JOUR. MED. SCI., 1913, cxlvi, 660.

observed it in cancer of the esophagus, though whether from metastasis in the bronchial glands or direct pressure on the bronchus was not known.

Increased whisper is much less common anteriorly, though it is occasionally heard over a considerable part of the sternum or along its border. It is sometimes present in the anterior axillary line just under the lower border of the pectoralis major muscle.

Several children in whom D'Espine's sign was present a few years ago, have improved much in health since coming under observation, and both the intensity of the whisper and its area of distribution are notably less.

Not only should one observe the quality of the voice, but auscultation should be performed when the patient coughs, for occasionally one will observe an echoing quality to the cough, even in the absence of whispered bronchophony.

D'Espine has had several autopsy confirmations of the value of whispered bronchophony in diagnosing enlarged bronchial glands. In a previous paper (Stoll³⁵), drawing attention to the value of whispered bronchophony in the diagnosis of tuberculosis in the aged, mention was made of finding enlarged glands in two adults who had had this sign. A third case has since come to autopsy. The complete history has been given elsewhere. The important points are as follows: Mrs. A. H., aged sixty-four years, had hemorrhage and cough "off and on" for many years, and with each attack she would "run down." The most noteworthy sign was the large area between the scapulæ over which D'Espine's sign was present. She died last winter, after a few days' illness, of a double pneumonia. The bronchial glands, especially the tracheal group, were much enlarged, as the accompanying photograph (Fig. 6) shows. No giant cells were found in either of two sections which Dr. J. C. Rowley kindly examined for me, though there was much pigmentation.

In only one case have we been able to compare the x-ray findings with a postmortem examination.³⁶ Louis G, aged two years, was admitted to the service of Dr. Charles Goodrich at the Hartford Hospital, May 28, 1912, because of enormously swollen cervical glands. Through Dr. Goodrich's courtesy the child was examined several times. There was dulness over the sternum and in the first three left interspaces as far out as the midclavicular line. Posteriorly well-defined dulness to below the spine of the scapula, extending $1\frac{1}{2}$ inches to the right of the spinal column and 1 inch to the left. The breath sounds were somewhat diminished and slightly tubular in quality. At the first examination the cry was

³⁵ Boston Med. and Surg. Jour., 1912, clxvii, 291.

³⁶ Since this article was written another case has come to autopsy. The x-ray being Fig. 7. There was advanced disease throughout right lung with large tuberculous bronchial glands. This will be reported later with photographs.

thought to be indicative of enlarged glands, but a note was made a few days later that there were "no auscultatory signs of enlargement of the bronchial glands." Yet, nevertheless, we felt that the glands were enlarged. Two months later, during which time the child had steadily failed, the dulnesses mentioned before had diminished very much, and a few scattered rales and small areas of bronchovesicular breathing had developed. The cervical glands diminished markedly in size during the last weeks of illness.

The *x*-rays showed the fine markings were very much increased, and extended to the periphery of the lung. Along the course of these interweaving thread-like lines were small dot-like shadows, giving the appearance of knots tied in thread. The largest of these were about the size of a pinhead. There was considerable increase in the shadow above the heart at the right root, which was incorrectly attributed to bronchial glands. As the picture was taken while the child was crying very hard and holding its breath, the shadow was probably a distended superior vena cava. In a second *x*-ray, taken just after death, this shadow was very much less.

The autopsy revealed no enlargement of the bronchial glands. The mediastinum was somewhat congested, and a few small tubercles were scattered throughout the lungs. A small group, the largest being pinhead in size, was found just under the pleura of the left upper lobe, and was apparently shown in the *x*-ray. The mesenteric glands were much enlarged and several were broken down.

It seems probable that the dulness noted anteriorly when the child first came under observation was due to an enlarged thymus, which decreased in size during the long illness, until at death scarcely a trace remained. The diminution of the dulness toward the last of the illness favors this theory. That the *x*-rays do not show thymic enlargement may be due to its being taken with the child on its back.

The impairment of resonance to the right of the upper thoracic vertebræ may have been the result of congestion of the hilus vessels.

It is conceivable that enlarged bronchial glands might have diminished in size coincidentally with the cervical group, but not that they should show no enlargement at autopsy.

The infection of the lungs was evidently hematogenous from a mesenteric or cervical gland, and death occurred before the bronchial glands were involved.

The venous hum heard over the upper part of the sternum when the head is retracted does not seem to be a sign of value.

As to the value of tuberculin, we are still of the opinion, expressed elsewhere,³⁷ that "Even when the tuberculin test is positive, we have to fall back on the symptoms to ascertain whether we are

³⁷ *Loc. cit.*

dealing with clinical tuberculosis which needs immediate treatment, or with only an anatomical lesion which requires temperance in all things."

RADIOGRAPHY. The large central shadow observed in the normal thorax is due to the heart and mediastinal contents. Extending out laterally are the heavy shadows caused by the large or stem bronchi. On the right side both ascending and descending bronchi are distinctly seen, but on the left, due to the intervention of the cardiac shadow, the greater part of the descending bronchus is not visible. The density of these shadows increases with age, being, as a rule, much heavier in the adult. Radiating from these coarser markings are finer lines which project into the lung field for varying distances, but do not extend normally to the surface of the lung. These markings are produced by the walls of the bronchi and the blood and lymph vessels with their contents.

Dunham and Boardman³⁸ found that in early tuberculosis these fine lines often reach the periphery of the lung at the site of the lesion. While our series of stereoscopic plates is small, in a number of instances we have observed this. In the infant with early military tuberculosis above referred to, which came to autopsy, the most distinctive feature was the filling of both lung fields with fine interweaving lines. In other cases where these lines did not extend into the lung field for any considerable distance, they were much more numerous and heavier than normal about the hilus region. In a few instances we have seen near the root small "soft" shadows with hazy irregular borders which are well shown in the stereoscopic negatives from which Fig. 8 is made. Fine lines can be seen connecting these shadows with the lung root. This is apparently an early involvement of the lung parenchyma in the hilus region. In non-stereoscopic negatives we have observed a shadow which is in the position normally occupied by the superior vena cava. This shadow is concave to the right, while the one caused by glands is convex, and is, moreover, of greater density, and protrudes farther into the lung field. It extends from the tip of the third cartilage upward toward the clavicle, giving an increased width to the root of the lung. Since drawing attention to this shadow in 1910³⁹ a number of other observers have mentioned it as an early evidence of enlarged bronchial glands. Involvement of the parenchyma in the hilus region is usually roughly wedge-shaped with the apex at the hilus. When the disease is but slightly active the shadow borders are usually sharp. In the more acute cases the shadow is softer and the border often ill-defined (acute exudative type of Cole). Because of the interposition of the cardiac shadow the infratracheal glands are usually not seen.

³⁸ Bull. Johns Hopkins Hosp., 1911, xxii, 229.

³⁹ Proc. National Association for Study and Prevention of Tuberculosis, 1910, vi, 252; also AMER. JOUR. MED. SCI., 1911, cxli, 83.

It is impossible for one who has not studied stereoscopic negatives to appreciate their superiority over the single plate method. While a lesion may be distinctly shown by the later process its exact situation cannot be determined. It is desirable for the

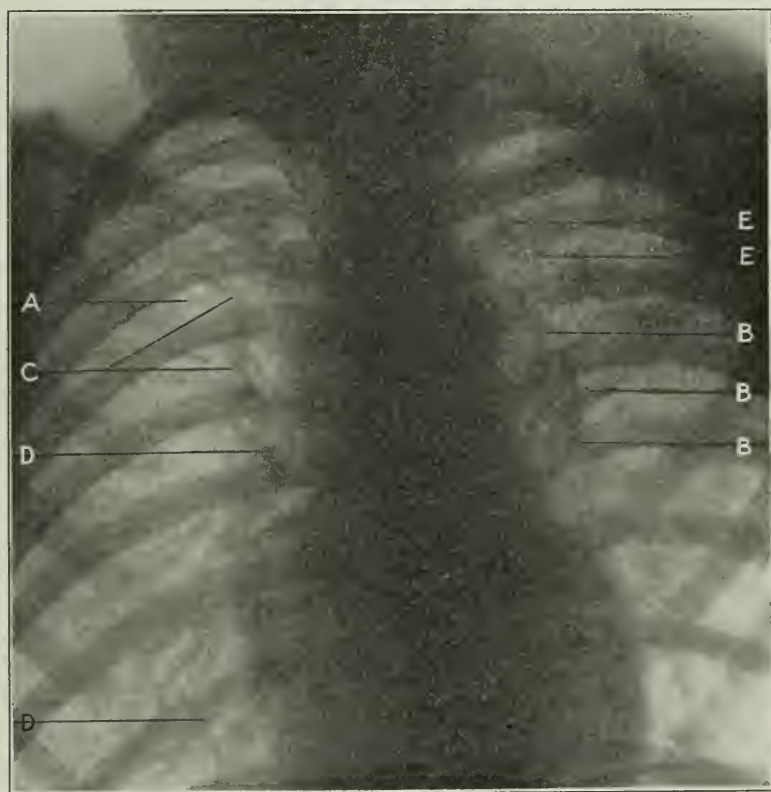


FIG. 8.—Stereoscopic appearance. (For physical signs see legend with Fig. 4.) Anterior view. The distortion of the mediastinal contents is due to the rotation of the chin to the right. In the upper lobe the fine lines approach almost to the lung surface, and in the first interspace there are two small tubercles just below the surface: A, at the left root are a number of tubercles which are arranged in three different layers resembling mountain ranges (B, B, B). In the lower part of the left upper lobe are observed several small shadows (E) of little density and with an ill-defined and irregular border. These are connected by fine lines with the root and are presumably early tuberculous foci. Posteriorly the finer markings extend to the surface of the right lung in the fifth (C), eighth, ninth, and tenth interspaces. A number of tubercles are seen at the root (D) and throughout the lower lobe.

clinician to learn to interpret his own radiographs, as only by this means can he satisfactorily compare his physical signs with the x -ray findings. All our cases were examined and the physical signs recorded before being radiographed.

TECHNIQUE. The method we find most desirable, and the one giving us the best soft-tissue detail, is as follows: With the patient in the erect position a moderately soft tube is placed approximately six feet from the plate (14 x 17 mounted in a screen). A small diaphragm is used and an exposure of one-half to one second is made. For stereoscopic work we use an automatic plate-changing device. The right oblique position has not proved very satisfactory.



FIG. 9.—J. L., aged seven years. Eczema as infant, whooping cough when one and a half years old, and ever since has had a cough. When first examined in 1909 had small moist rales over upper two-thirds of both lungs. Well-marked d'Espine and a small area of bronchovesicular breathing at the inferior angle of left scapula. The rales have cleared up except a few at both bases, and the most marked whisper is heard just internal to inferior angle of left scapula. Stereoscopic appearance: The right descending bronchus is much heavier than normal. An increase of lines from right apex to root (A) is to be observed and a haziness of the whole of the apex. The fine lines extend to the surface of the lung in the third, fourth, fifth, and sixth (B) interspaces left and the first, second, third, and fourth interspaces of the right side when viewed from behind, but in the anterior view the line markings do not reach the surface. The fine lines at the lung root are increased. Several tubercles can be seen at C.

TREATMENT. When diagnosed early the usual out-of-doors treatment for tuberculosis will usually suffice. Children so affected should attend an open-air school, as there are few environments more disastrous to health than the usual overheated, unventilated school-room. In several instances we have given tuberculin therapeutically with seemingly good effect. One child in particular, whose cough at night was very distressing, experienced great

relief from tuberculin treatment. Interruption of the treatment was followed by a recurrence of the cough, which again became less upon the resumption of tuberculin. This sequence of events was repeated several times, as it was impossible to make the mother realize the necessity of keeping up the treatment. Dr. H. W. Brayton made a number of blood-counts before and after the



FIG. 10.—Stereoscopic appearance. L. H. (For physical signs see legend with Fig. 5.) Anterior view. The fine lines (A) extending upward from the left root to the apex are somewhat increased and slight cloudiness to the whole left apex (B) above the clavicle. At the right root, opposite the third rib, an enlarged bronchial gland (C) can be seen in which are a number of tubercles. The lines radiating from the right root, especially those standing downward, are heavier and more numerous than usual. None of the fine lines extend to the surface in the anterior view, but when examined from behind the fine lines extend to the periphery in the fifth interspace. The clinical diagnosis was "involvement of the bronchial glands and right root." The lesion at the left apex was not recognized, though it should have been because of the harsh inspiration and muscle spasm.

tuberculin injection, and did not observe that the lymphocytes were increased after the tuberculin injection, as Schulz⁴⁰ claimed they were.

When the lung adjacent to the glands is shown by means of the x-rays to be involved, Straub and Otten⁴¹ advise making an artificial pneumothorax.

The gradually increasing dyspnea is difficult to deal with. Believing that he was operating for the relief of the dyspnea from

⁴⁰ Beitr. z. klin. d. Tuberk., 1911, xxi, 79.

⁴¹ Loc. cit.

an enlarged thymus, Veau⁴² exposed a mass of caseous bronchial glands, which he removed. Betke⁴³ also operated successfully on a woman, aged twenty-nine years, who had tracheal stenosis from tuberculous glands at the bifurcation of the trachea.

It is possible that with the more general adoption of one of the methods by which the thoracic cavity can be explored with impunity, operative relief in these cases will become the rule.

Such excellent results have been obtained in thymic dyspnea by x-ray treatment, that it seems it should be thoroughly tested in enlarged bronchial glands.

Mention has been made of the relief of the dyspnea from the passage of the bronchoscope. This can only take place when the dyspnea is due to actual pressure of a gland on the trachea, and it is a procedure of much hazard, for if the instrument should perforate the already bulging and diseased tracheal wall the result would probably be disastrous. As the dyspnea in most cases is the result of a vagus neuritis rather than a mechanical pressure, it would seem that the usefulness of the bronchoscope in these cases is not great.

The urgent dyspnea from the rupture of a gland into a bronchus or trachea calls for immediate relief. If the patient is not able to expel the disintegrated gland by coughing, a tracheotomy should be performed and a large catheter, with the end cut off, so that the opening is at the end, passed downward. In the cases where the obstruction is due to pus, aspiration might be life-saving. In Goodman's case, insufflation caused the pus to be discharged through the tracheotomy wound by the sides of the tube.

CONCLUSIONS. 1. Prior to the fifteenth year, tuberculosis of the bronchial glands and lung hilus is the most common form of tuberculous disease.

2. The early symptoms are usually indefinite and chiefly of toxic origin. While a cough is generally present, it may be entirely absent even with advanced disease of the bronchial glands.

3. Although the orthodox signs of incipient (apical) tuberculosis are not present in these cases—in fact, the primary lesion is often in the lower lobe—there are certain physical signs which are indicative of a pathological process at the lung root.

4. The significant signs are a "hilus dimple" (noted anteriorly over the hilus region at the end of inspiration), dilated veins, parasternal and paravertebral dullness, and most significant of all, a well-marked whispered bronchophony in the interscapular region (d'Espine's sign).

5. Radiography, and especially stercoradiography, is of the utmost value in these cases, as it shows the exact location and extent of the morbid process, and is the greatest stimulus to careful clinical work.

⁴² Bull. Soc. de pediat. de Paris, 1911, No. 2, p. 83.

⁴³ Berl. klin. Woch., 1913, No. 4, p. 197; quoted by Goodman, *op. cit.*

HEREDITARY ATAXIA.

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THE hereditary ataxias form a large and important group of nervous diseases, the accurate subdivisions of which often cause uncertainty and confusion. The various types, such as the spinal ataxic paraplegia, Friedreich's spinal ataxia, and Marie's cerebellar ataxia may combine enough symptoms of each form to make the definite grouping most difficult.

The cases reported in this paper show this tendency and cannot be definitely placed in either group, though resembling most the cerebellar type of Marie. The spastic, springing, or bouncing gait with some degree of ataxia is most peculiar and the extent of the athetoid and choreiform movements with the decided ataxia of the muscles of the face, tongue, and throat, the extremely ataxic speech, and the late onset of the disease, are all out of the ordinary.

The spinal type of hereditary ataxia described by Friedreich develops usually before the age of puberty, in most cases about the age of ten years. The history is generally one of a steadily increasing clumsiness first noted in the child's running and jumping during his play. This gradually increases, and choreic and at times athetoid movements develop, most active in the arms, but often including the head, and causing a peculiar purposeless bobbing or nodding of the head. Nystagmus occurs, the speech becomes slow and drawling and later ataxic, and the patient's mentality deteriorates; this latter, however, is not so frequently true as in the cerebellar type.

Ordinarily sensory changes are not present, though later observers record some loss in position sense, compass point discrimination, etc. The bowel and bladder are unaffected. The patellar reflexes are often absent and Romberg's sign is positive. Scoliosis and deformities of the feet and legs, with the characteristic Friedreich's toe, may occur and are seldom found in the other forms. Tremor of the hands, tachycardia, excessive sweating, and fragilitas ossium are some of the less common symptoms and really not characteristic of the disease.

In the cerebellar type described by Marie, Fraser, and Nonne the symptoms often resemble very much those of Friedreich's disease, and the two may be combined clinically and pathologically, one or the other form preponderating. In Marie's cerebellar ataxia the symptoms are more those of cerebellar involvement, such as the staggering, drunken gait, explosive ataxic speech, ataxia of the

extremities, etc. The onset is later, usually after the age of puberty; spastic ataxia and paraplegia are absent or occur late in the disease, while the ataxic speech defect, mental deterioration, and jerky tremors are more apt to be prominent symptoms of the cerebellar form. Optic neuritis is not uncommon. The knee-jerks are preserved and, as a rule, active. There is no decided Romberg swaying in typical cases.

In the hereditary ataxias the spinal cord or the cerebellum, or both, as the case may be, show congenital underdevelopment. In addition the lateral and posterior columns of the cord are sclerosed in Friedreich's ataxia, while in the cerebellar type the principal findings are atrophy and sclerosis of the cerebellum. Pathological changes have also been reported in the cerebral cortex, the meninges, and in the cells of the spinal cord.

Where the lateral columns of the cord are more or earlier affected the case may be grouped under the spastic ataxic paraplegias; the speech defects, bone deformities, etc., are uncommon in these types. It is, however, only a subclass of the Friedreich group and would better be considered as such.

Cases of juvenile tabes and the neural type of progressive muscular atrophy and multiple sclerosis have some symptoms in common with the hereditary ataxias and might lead to some difficulty of diagnosis in the earlier course of the diseases. Like most hereditary diseases the hereditary ataxias are transmitted more often by the female members of the family. Direct inheritance from one generation to the next is not very common, but in most cases the intermediate family or generation show other forms of degeneracy, such as epilepsy, insanity, imbecility, etc. Nothing can be done for the direct betterment of these patients other than temporarily making them as comfortable as possible and relieving any unusual symptoms. The disease once developed steadily progresses, very occasionally, however, showing a long retardation of the symptoms. Any definite help to families so affected can only be along a eugenic line.

CASE I.—J. D., aged fifty years, farm laborer up to six years ago; married. Eight children living and well so far as he knows; five boys and three girls. Three healthy brothers, aged thirty, thirty-seven, and forty years, and one similarly affected. Maternal grandfather had same disease; time of onset not known. His mother had the same trouble; date of onset not known. She died aged fifty-three years. Patient's first symptom started when he was aged forty-four years, as a general clumsiness.

During the examination the patient would require two or three minutes to answer a simple question, during this time making an intense effort to speak. He would move his arms, shoulders, and legs, elevate the eyebrows, move his mouth, roll his eyes, and finally answer in a slow, broken, drawling, ataxic manner.

His mouth and tongue movements were ataxic and the rolling of the tongue and twisting of the mouth could be seen during his efforts to shape them for a reply. Sometimes he would struggle so long that he would forget the question.

He says it is more difficult for him to walk at night, though he did not show any increased swaying upon closing his eyes when his station was tested.

The pupils were equal and reacted normally. No nystagmus. The finger-to-nose test and the heel-to-knee tests showed some ataxia, but not nearly so much as might be expected. The deep reflexes of upper and lower limbs were all exaggerated.

His gait resembled somewhat that of a tabetic. The legs would be swung forward in the flail-like manner, but the toes would be held up and the knees would extend sharply, causing a peculiar bounding or springing effect. The arms would be held in extension backward, possibly as a partial balance, and the body flexed forward at the waist or hips. The arms jerked and the movements of the facial muscles would continue while the patient walked. While sitting, supposedly unobserved, the movements were not present, nor during sleep, and he could often stand quietly.

There were no sensory changes in either brothers. The sense of position may have been affected, as neither of them could use their hands very well, and they had great difficulty in eating and even in playing cards.

Never any incontinence of urine or feces. Impotent for about ten years.

At intervals of a few seconds to a half-minute the patient would roll his eyes and close his eyelids and turn his head slightly, resembling somewhat a tic movement.

CASE II.—D. D., aged forty-three years; farm laborer. Disease began about five years ago. Is a brother of Case I. Married and has five healthy children.

The symptoms in this case resembled very much those of his brother. His gait had more of the peculiar bouncing, mechanical character, and his condition is in general much further advanced.

In answering or attempting to answer questions the ataxia of the face and tongue was so extreme that he could not pronounce his name. In these attempts the mouth would be held open and the tongue could be seen rolling about in his ataxic effort to speak. All parts of his mouth could not be closed at once, so that his speech was often mumbling and indistinct. During his efforts he would hump his back and work his eyes and facial muscles.

The pupils reacted normally to light and accommodation. No nystagmus. Often the patient in trying to keep his eyes open would spasmodically close them. (In repose both brothers appeared to have ptosis.) Attempts to protrude the tongue would show great lack of control and ataxia; the patient would wag his tongue,

partially protrude it, and quickly pull it back, this continuing for four or five or more times before he could hold it out. The face could not be drawn up at the side voluntarily by either brother.

The deep reflexes were exaggerated but no Babinski. No sensory changes, either objective or subjective.

Finer movements, as in eating, etc., were impossible or most difficult.

Ataxia in knee-, heel-, and finger-to-nose tests was well marked. The patient could neither sit nor stand quietly. In this respect both patients resembled very much cases of Huntington's Chorea. Had incontinence of urine four or five times about ten years ago. He says his sexual power is not impaired.

CHOLESTERIN ANTIGENS IN THE WASSERMANN REACTION AND THE QUANTITATIVE TESTING OF SYPHILITIC SERA.

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1. CHOLESTERIN ANTIGENS. The addition of cholesterol to lecithin solutions or to alcoholic organ extracts used as "antigens" in the Wassermann reaction was first recommended by Browning, Cruickshank, and M'Kenzie, and later by Sachs, Walker and Swift, and others. The experience of all has been that such preparations give fixation of complement with many syphilitic sera which fail to react with similar extracts without the cholesterol. Walker and Swift tested the sera of twenty-two individuals in whom syphilis could reasonably be excluded with cholesterol-heart extract preparations and obtained no fixation except when an excessive amount of the extract was used, in which case some of the sera gave partial fixation. Recently, Thomas and Ivy have reported a number of false positive reactions obtained with these antigens. It should be noted, however, that they used only the minimal hemolytic dose of amboceptor and complement, a practice which of itself makes the test extremely sensitive and also unreliable, according to the experience of most workers.

The advantage of using antigens which will increase the number of positive reactions is obvious, providing there is reasonable certainty that the antigens will not react with non-syphilitic serum. However, some procedures which increase the delicacy of the reac-

tion, such as testing the serum without previous inactivation or using minimal amounts of complement and amboceptor, have been found to give non-specific reactions, and it seemed possible that such might be the case with the cholesterol antigens. For this reason we determined to test their sensitiveness and reliability by using them in a series of routine examinations, testing the same sera simultaneously with extracts possessing known properties.

The Wassermann reactions were carried out with one-half the original amounts: that is, 0.1 c.c. of patient's serum, 0.5 c.c. of diluted antigen, and usually 0.05 c.c. of guinea-pig serum (the exact amount being determined each day by preliminary titration) in the first stage, and 1 c.c. of 25 per cent. sheep cells sensitized with twice the minimal hemolytic dose of immune rabbit serum in the second stage. In testing spinal fluids 0.5 c.c. was used. Controls for anticomplementary action, one containing double the amount of serum (or spinal fluid) and one containing double the amount of antigen used in the test were always made. When the controls showed any inhibition the tests were disregarded.

The extracts were prepared by treating chopped moist guinea-pig heart with absolute alcohol for two to three weeks at 37° C., the proportions being 1 gm. of tissue to 10 c.c. of alcohol. To the filtered extract 0.4 per cent. cholesterol was added, and after this had stood for twenty-four hours in the incubator the undissolved residue was filtered off. This method is that recommended by Walker and Swift, except that guinea-pig heart was used instead of human. Emulsions for use in the tests were prepared by adding salt solution, at first drop by drop and then rapidly, to the alcoholic extract, the mixture being shaken during the process. A few tests were made with emulsions prepared in the reverse manner, the alcoholic extract being dropped into the salt solution, but the results seemed less satisfactory. Sachs and Rondoni found, in regard to simple alcoholic extracts, that dilutions made in the latter way were less anticomplementary but proportionately still less active as antigens, and consequently less satisfactory than the more turbid emulsions produced by the slow addition of salt solution to the extract. This has also been our own experience. The anticomplementary power of all the extracts was determined before use, and it was found that most of them produced slight inhibition in amounts from 0.1 to 0.12 c.c., but none in amounts of 0.08 c.c. or less. In performing the reactions one-fourth of the largest amount which showed no inhibition was used—usually 0.02 or 0.025 c.c.

In the control series of tests the acetone insoluble lipoids of beef-heart extract, prepared by Noguchi's method, were used as antigen.

The reactions obtained with sera from 475 patients and with 50 specimens of spinal fluid are shown in Table I.

TABLE I.

Condition.	Number of cases.	Lipoid antigen. Number of positive reactions.	Cholesterin antigen. Number of positive reactions.
Blood-serum:			
Primary syphilis	10	6	7
Secondary syphilis	25	21	25
Tertiary syphilis	99	59	79
Congenital syphilis	9	5	7
Tabes dorsalis	20	9	13
General paresis	4	4	4
Latent or cured syphilis	44	17	29
Apparently non-syphilitic	264	4	25
Spinal fluid:			
Tabes dorsalis	19	8	10
General paresis	3	3	3
Tertiary syphilis	9	3	2
Non-syphilitic	19	0	1

In tabulating our results we have recorded as positive only those of the tests which showed no or very slight hemolysis after an hour's incubation in the second stage. When using the lipoid antigens all tests showing 50 per cent. or less hemolysis may safely be called positive, and such readings would give a somewhat larger proportion of positives with these antigens in luetic cases than the table shows. Many non-luetic sera, however, gave partial inhibition of hemolysis with the cholesterin-heart extract preparations, and better results were obtained with these if only those sera which caused practically complete inhibition were regarded as positive.

The cases are grouped in the table according to the clinical diagnosis. Many cases which seemed doubtful have been disregarded; but, even so, the probability of some errors in diagnosis must be considered before conclusions are drawn from these figures. One difficulty is that the diagnosis in many cases was doubtless influenced by the result of the Wassermann reaction. As a matter of fact, cases giving an indefinite history of lues with a positive serum reaction have been included under the head of "latent syphilis," whereas cases giving a negative reaction were not considered to be syphilitic unless the history or clinical picture was fairly characteristic of the disease.

Of the 525 reactions which have been included in the series the result was the same with both types of antigen in 455. Only two specimens which were positive with the "lipoid" antigen were negative with the "cholesterin." These were both spinal fluids, one from a case of tabes and one from a case of cerebrospinal syphilis. On the other hand, 68 specimens reacted positively with the "cholesterin" antigen, but not with the "lipoid;" of these cases 46 were syphilitic and 22 apparently non-syphilitic. Of the former, 3 were treated secondary cases and 1 an untreated secondary; but the majority were tertiary or latent cases. Of the 26 which have been classed as non-syphilitic, 1 was a case of sarcoma, 4 were cases

of carcinoma, and 4 cases of pernicious anemia. One was a case of estivo-autumnal malaria, a condition in which positive Wassermanns have frequently been reported. The other cases represented a variety of conditions, many of them local infections; but except for the cases mentioned these false positive reactions were not found twice in the same disease, and there seems no reason to believe that the illness of the patient at the time was responsible for the result of the test. The Wassermann reactions were not made as a routine on all admissions, so that in nearly all these cases which we have classed as probably non-syphilitic the possibility of lues was considered at the time the tests were made. In several instances, however, the nature of the suspected gumma or ulcer was determined by histological examination; and in the remainder, further observation ruled out syphilis so far as the present illness was concerned. It is, however, impossible absolutely to exclude latent syphilis in these cases. Four cases that were clinically non-luetic gave reactions with both types of extracts used. It is certain that the "lipoid" antigens rarely, if ever, give false positive reactions, and it is probable, therefore, that these patients had unrecognized infections. It seems highly improbable, however, that 25 out of 264 patients, or 9 per cent., presenting no history or signs of syphilis, should in fact be luetic.

A factor which probably accounts for some of our non-specific reactions is the instability of these extracts. A number of the false positive tests were obtained with a preparation which was over six weeks old. At this time it was found that the anticomplementary power had increased very considerably, and although the amount used in the reaction was proportionately decreased, a number of positive tests which could not be explained by the clinical data were obtained. In view of this experience, antigens less than four weeks old only were subsequently used, with considerable improvement in the results. As the presence of a slight excess of antigen also seems to produce non-specific reactions the making of an anti-complementary control containing four times instead of twice the amount of antigen used in the test is recommended.

In spite of the apparently false reactions obtained, we believe that these extracts are of distinct value on account of the large number of positive results obtained in tertiary syphilis and in cases cured so far as symptoms were concerned, which failed to react with the "lipoid" antigens. There are obvious advantages in so sensitive a test in controlling treatment, or in cases where it is desired to exclude syphilis so far as possible, as, for example, in selecting donors for blood transfusion or in examining wet-nurses. The reactions are also very helpful in diagnosis when there is some clinical evidence in their support.

It should be remembered, however, that the nature of the Wassermann reaction is not known and that it is essentially empirical.

Until it can be shown by long experience, therefore, that these extracts do not react with non-luetic sera they should not replace extracts whose reliability has been established. What evidence we have been able to obtain indicates that they do give complement fixation with some non-syphilitic sera. It would seem advisable, then, in routine work to test all sera both with a sensitive cholesterin preparation and with some less sensitive but thoroughly reliable extract.

2. THE QUANTITATIVE TESTING OF SYPHILITIC SERA. Another phase of the Wassermann technique which has interested us has been the determination of the strength of the reaction in positive sera. This is specially important in following cases under treatment. The most logical method is to make tests with various amounts of the serum, to determine how small an amount will produce the reaction. In order to measure the small amounts required at least two preliminary dilutions of each serum to be tested must be made, and this very considerably increases the labor of carrying out a large series of reactions. In some laboratories this difficulty is avoided by testing constant amounts of serum against serial dilutions of the antigen, which can be prepared in bulk for all the tests to be made on a given day.

A technique based on this principle was introduced by Coca and l'Esperance, and in their hands gave excellent results, and we have followed their procedure with slight variations in making some five hundred Wassermann tests. The reaction is carried out with one-tenth the volume used in the original Wassermann method. The patient's serum (unheated) is first diluted with four parts of salt solution, and 0.1 c.c. is placed in each of five tubes; in a sixth tube 0.2 c.c. is placed for a control. As antigen a 2 per cent. solution of the acetone insoluble fraction from normal beef-heart extract prepared by Noguchi's method is used. Emulsions are prepared containing 0.05, 0.025, 0.012, 0.006, and 0.003 c.c. of this stock solution per cubic centimeter, and each serum is tested with 0.1 c.c. of each of these dilutions; $\frac{1}{10}$ c.c. of a 1 in 10 dilution of guinea-pig serum is used in the test, with 0.1 c.c. of a 5 per cent. emulsion of sheep corpuscles and two units of hemolytic amboceptor.

The use of the patient's serum without previous inactivation is thought by some workers to be a safe procedure, provided that antigen free from protein constituents is used, although it is admitted that false positives are obtained with simple alcoholic organ extracts. Although in our tests a carefully prepared "lipoid" antigen was used, positive reactions were obtained in a few cases in which there was no evidence of syphilis other than this reaction, and in which the inactivated sera were negative both with "lipoid" and with "cholesterin" antigen. While some sera from tertiary and latent cases reacted positively in fresh condition, but not when inactivated, four sera which when active gave negative results, after inactivation

TABLE II.—Estimates of Strength of Sera Obtained by Various Methods, Compared.¹

	(a) Sera tested in graded amounts against 0.02 c.c. of lipid antigen.					(b) Sera tested in graded amounts against 0.05 c.c. of cholesterol antigen.					(c) Same sera tested in constant amounts (0.1 c.c.) against graded amounts of lipid antigen.					(d) Same sera tested in constant amounts (0.1 c.c.) against graded amounts of cholesterol antigen.				
	Amount of patient's serum.					Amount of patient's serum.					Amount of antigen.					Amount of antigen.				
	.1	.05	.025	.0125	.0062	.1	.05	.025	.0125	.0062	.02	.01	.005	.0025	.00125	.05	.025	.0125	.0062	.0031
1. Secondary	0	0	0	++	++++	0	0	0	++	++++	0	0	0	0	0	0	0	0	0	0
2. Tertiary	++	++	++++	++++	++++	0	+	+	++++	++++	++	++++	++++	++++	++++	0	0	0	0	0
3. Tertiary	0	0	0	0	+	0	0	0	0	0	0	0	+	++	+++	0	0	0	0	+
4. Tubes	0	0	0	+	++++	0	0	0	++++	++++	0	0	0	0	0	0	0	0	0	0
5. Secondary	0	0	0	++++	++++	0	0	+	++++	++++	—	0	0	0	—	0	0	0	0	0
6. Latent	0	0	0	++	++++	0	0	+	++++	++++	0	0	0	+++	++++	0	0	0	0	0
7. Tertiary	0	0	0	++	++++	0	0	0	+	++++	0	0	0	0	++	0	0	0	0	0
8.	0	+	++++	++++	++++	0	+	++++	++++	++++	0	0	+	++++	++++	0	0	0	0	0
9. Latent	0	0	0	++	++++	0	0	0	0	0	0	0	0	0	0
10. Latent	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11. Latent	0	0	0	0	+	0	0	0	0	0	0	0	0	0	0
12. Tertiary	0	0	0	0	+	0	0	0	0	0	0	0	0	0	0
13. Tertiary	0	0	++++	++++	++++	0	0	0	0	++++	0	0	0	0	0
14. Tertiary	0	0	0	++	++++	0	0	0	0	0	0	0	0	0	0

0 = no hemolysis.

++++ = complete hemolysis.

¹ The cholesterol antigens in this experiment were in clear emulsion, obtained by adding the extract to the diluent drop by drop. Consequently, relatively large amounts were used.

gave positive results with the same antigen. These negative reactions were probably due to the complement in the patient's serum. The results make the employment of active serum appear distinctly disadvantageous. Moreover the small quantities used in this technique introduce the possibility of error on account of the care required to deliver 0.1 c.c. accurately from the blunt-tipped pipettes which are usually employed in this work.

The method was chiefly interesting, however, as a means of determining the strength of the reaction. The majority of the sera which reacted at all gave complete inhibition in at least four of the five tubes set up. For example in tertiary cases, where weaker reactions would be expected, out of 60 positive sera, 27 reacted in the fifth tube containing one-sixteenth of the usual amount of antigen, and 41 reacted in the fourth tube of the series. As so many specimens reacted alike the method did not give a very satisfactory grading of their strength. A series of higher dilutions would doubtless have brought out further differences. It has been asserted by MacIntosh and Fildes that titration with varying amounts of antigen does not give an accurate estimation of the strength of the reaction. They base this assertion on experiments in which the same sera were titrated, using varying amounts of serum with constant amounts of antigen, and also using constant amounts of serum with varying amounts of antigen. We tested in this way fourteen sera, using the "lipoid" type of antigen, and eight with the "cholesterin" type also, as shown in Table II.

The titrations in which the amount of serum was graded (*a* and *b*, Table II) with both antigens showed considerable variations in strength among the sera used. When titrated in the reverse way with the less sensitive antigen (*c*) the relative values did not run parallel, and the differences between them were much obscured; while with the more sensitive antigen (*d*) these differences were lost almost altogether.

It seems then that a closer estimate of the strength of syphilitic serum may be obtained by determining how small a quantity of it will produce a reaction, rather than by determining with how small an amount of antigen it will react; or, in other words, that quantitative Wassermann tests should be made by varying the amount of serum used, and not the amount of antigen.

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AN UNATTACHED MASS FOUND IN THE ABDOMINAL CAVITY OF A MALE.

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INASMUCH as the following case report is extraordinary, it is of interest, but insofar as it raises the question of intra-abdominal growth without obvious nourishment, it is perhaps of more scientific importance. It is, therefore, best to leave any discussion until the facts are portrayed.

A. McL., aged sixty-nine years, was admitted to the Montreal General Hospital November 10, 1912. He had suffered from digestive disturbances for forty years, more or less, complaining chiefly of constipation, a burning sensation in the stomach after eating, and of distention and discomfort from gas in the bowels. There was no nausea or vomiting. Two or three years ago he had attacks of pain in the region of the appendix, which called on one occasion for morphin. He did not vomit in these attacks.

For a period of about twenty-five years he can remember a mass in the right side of the abdomen, which at first was quite small, smaller than a hen's egg, and was always freely movable, so movable that it would disappear, apparently into the pelvis, for two or three days at a time. He could push it into any part of the abdomen he wished, but it was first found in the right hypochondrium, and he was most comfortable when it remained in that situation. It always tended to follow the laws of gravity, and in consequence was generally to be found in the most dependent part of the abdomen, falling from side to side as he turned in bed. He had the impression that it was a floating kidney, and indeed he had been told by his medical advisers that this was the most probable diagnosis. The urine, however, had until recently never shown any pathological changes, nor had he suffered any renal crises. He had had pain in the region of the right hypochondrium of a more or less indefinite nature.

We had an opportunity of discussing the case with his physician, who had noted the mass when he first examined him six years previously. It was then the size of a large hen's egg, and of the present consistence. It had, to his certain knowledge, increased

in size to its present dimensions, which may be described as those of a large orange or a small grapefruit.

The patient came to the Montreal General Hospital on account of an attack of cystitis, with retention, which he had developed in consequence of an hypertrophied prostate gland.

On examination he was found to be a spare, rather pale old man, with little or no subcutaneous fat; arteries moderately sclerosed; normal lungs and heart; rather anemic, and altogether frail. His urine contained considerable pus, and he suffered almost complete retention, due to a moderately hypertrophied prostate gland.

The abdomen was scaphoid, the umbilicus prominent, and the walls soft and non-resistant, making palpation easy. In the right upper quadrant was a hard, slightly irregular mass the size of a large orange. This could be turned about so as to present slightly different aspects to the examining hand, could be pushed downward, and even across the spine to the left side without any trouble, and would stay where placed. It was too large to go down into the pelvis, but this was the only apparent reason why it should not do so, it was so freely movable.

An α -ray examination gave no shadow. It was not tender. It was dull on percussion, and was evidently situated in front of the bowels. It was not kidney, but the kidneys were not palpable. The two most marked features about it were its extreme mobility and its marked hardness. The diagnosis of an omental tumor was made.

OPERATION.—The patient was not a good operative risk, owing to the infection of his urinary tract, which apparently involved the kidneys. He was, therefore, put upon catheter life, with daily bladder lavage. So anxious was he, however, that something should be done for the abdominal condition, and so simple did the operation appear, that on November 18, 1912, under gas and oxygen anesthesia, the abdomen was opened directly over the mass, which had to be held stationary by an assistant. In cutting through the peritoneum, we came at once upon the tumor, which showed a pearly white glistening surface, exactly comparable to a uterine fibroid. Pressure on either side of the wound caused the mass to pop out of the wound on to the abdominal wall. It had absolutely no pedicle, nor any attachment whatever. It bore no apparent relation to any viscus, nor was there an adhesion of any kind attached to it. Indeed, on searching the abdomen there did not seem to be any adhesions present. There was, however, a small amount of fluid about the loops of small bowel. The wound was closed, and the patient did well for the next seven or eight days, when he began to fail, with frequent attacks of vomiting and hiccough. The wound, however, remained normal, and it was evident that the lesion was outside the peritoneal cavity. He died January 6, 1913, forty-eight days after the operation.

The autopsy protocol is as follows:

Montreal General Hospital, 13.8, January 7, 1913. Ten hours postmortem.

The body is that of a poorly developed, much emaciated male adult. No edema is present, but considerable lividity of the dependent parts. Rigor mortis is marked.

Abdomen. There is an elevated bluish scar in the middle line, between the umbilicus and the ensiform cartilage, 13 cm. in length (operation wound).

Peritoneal Cavity. The peritoneal cavity shows no excess of fluid. The peritoneum is smooth and shiny, but darkly pigmented on both parietal and visceral layers. Mesentery is bluish-black. Mesenteric glands are slightly enlarged and darkly pigmented. There are extensive general fibrous adhesions in the abdominal cavity between the liver and colon, the spleen and colon, and binding down the cecum to the posterior abdominal wall. The appendix is retrocecal, surrounded by fibrous adhesions. In one of the fibrous adhesions between the transverse colon and the under surface of the left side of the diaphragm is found a hard calcified mass 0.5 cm. in diameter. It is not attached to the mesentery. A similar mass, perfectly spherical, measuring 0.7 cm. in diameter, is found under the peritoneum of the small bowel about 36 inches above the ileocecal valve. This body is white and calcified, with a smooth surface under glistening peritoneum, and is 2 cm. from the mesenteric attachment (Fig. 1).

Pleural Cavity. This contains no excess of fluid, but there are extensive fibrous adhesions on both sides.

Pericardial cavity. The pericardial cavity contains no excess of body fluid. There are extensive adhesions, delicate and recent, and firm and old between both layers of the pericardium.

Heart. The heart is 320 gm. in weight. It is pale brown on section, and the muscle is soft. The endocardium is normal. The aortic arch shows some raised whitish discoloration. The coronary arteries are patent and show a moderate degree of atheromatous change.

Lungs. The right upper and lower lobes are full and firm to the touch. On section they are of a general grayish, mottled appearance. There are many raised gray areas alternating with edematous lung tissue. Even on gentle pressure, much pus and purulent fluid exudes from these areas. The right middle lobe is dark red in color and edematous. The upper and lower lobes are nodular and uneven to the touch. The lower lobe on the left side presents a similar condition to that of the upper and lower lobes on the right side. There are several old pleural scars at the apices of both sides, but no calcareous or caseous nodules are found.

Spleen. Normal.

Stomach. Normal.

Intestines. Normal.

Pancreas. Normal.

Liver. Weight, 1580 gm. It shows on the under surface of the right lobe, retroperitoneally, an area 10 x 6 cm., which forms one of the confines of the large, perinephritic abscess described below. Otherwise the organ shows nothing abnormal.

Kidneys. The right kidney weighs 300 gm. There is a perinephritic abscess cavity connected with the upper pole of the kidney, and extending upward to the liver. This cavity measures 12 x 6 x 10 cm., and is filled with a greenish-brown purulent fluid. The right kidney shows extensive abscess condition throughout. The right ureter is thickened, and the mucous membrane is red



FIG. 1.—Small subperitoneal calcareous nodule found in the small bowel.

and granular. The left kidney is more normal. The cortex averages 0.3 cm. in thickness. The capsule strips with difficulty, and leaves an uneven surface, which shows some retention cysts. The vessels are tortuous. There is no sign of infection.

Right Adrenal. The right adrenal cannot be found, but the left is normal.

Bladder. The bladder is much thickened and trabeculated, with a pigmented and granular mucosa.

Prostate. The prostate is large.

Aorta. The aorta shows marked atheromatous degeneration, especially about the origin of the intercostals.

ANATOMICAL DIAGNOSIS. Pyonephrosis; perinephritic abscess (right); acute and chronic pericarditis; bronchopneumonia; chronic cystitis; chronic nephritis; calcified nodules, subperitoneal; hypertrophied prostate.

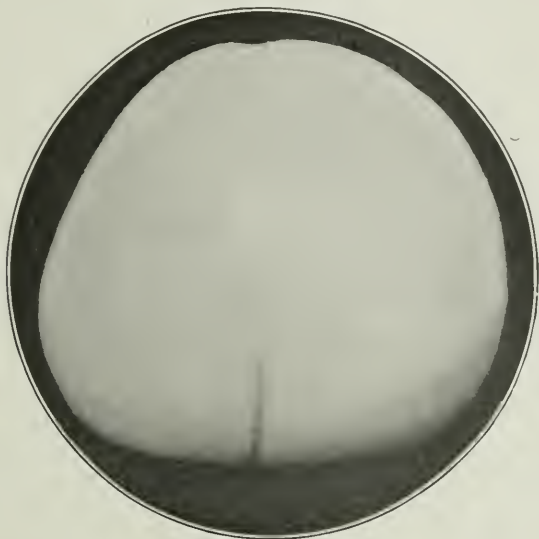


FIG. 2.—View of the mass as removed from the abdominal cavity, about two-thirds actual size.



FIG. 3.—View of mass on section, showing calcareous centre, but not the concentric arrangement of layers.

HISTOLOGICAL EXAMINATION. Montreal General Hospital, S., 12, 635, November 18, 1912.

The tumor is roughly spherical in shape, but with three flattened surfaces or facets (Fig. 2). It measures 9 x 8 cm. in diameter, and has a smooth, white, glistening surface, without pedicle or any adherent tissue. It is very firm. On section, the mass cuts with some difficulty, and is seen to have a calcareous centre, 1.5 cm. in diameter (Fig. 3). The sectional surface is, for the most part, white and very firm, but an occasional darker ring or lamella accentuates a concentric formation, which is evident in both diameters. The tissue immediately around the calcareous centre is somewhat softer than the remainder.

Sections cut from the mass in various regions show a tissue composed of laminated branching fibers, which take a homogeneous color with methylene blue, and the various differential stains employed. No vessels, cells, nuclei, or fibrils can be demonstrated. In the centre of some fibers, a fine granular deposit is noted, probably calcium salts.

To establish the identity of the tissue is difficult. Were it the remains of a true fibroma, one would expect evidences of vessels, or at least spaces, to persist. The question arises whether it is simply fibrin which has been deposited, layer after layer, on whatever originally was the nucleus, or whether it is collagen remaining from organization of layers of fibrin, similarly deposited by fibroblasts, which have subsequently disappeared, leaving resistant collagen lamellæ.

The tissue takes a homogeneous blue stain with Mallory's connective-tissue stain, and pink with phosphotungstic acid hematoxylin. These are the reactions for collagen. To try and further rule out fibrin, an attempt was made to digest the tissue with pepsin, controlled by the digestion of fresh fibrin, and formalin fixed fibrin (the tumor tissue having been fixed in formalin), but neither the formalin-fixed fibrin nor the tissue fibers were digested.

Certain facts seem worthy of reiteration:

1. The tumor had been present twenty years or more, and had been noted by the patient's present physician six years ago.

2. It had always been freely movable.

3. It had never caused pain, other than a feeling of discomfort from moving about.

4. It had grown steadily and slowly from a small nodule, which frequently disappeared for days, to a tumor too large to enter the pelvic inlet.

5. Operation showed it to be absolutely unattached, either by pedicle or by a surrounding envelope of omentum or adhesion.

6. There is no evidence that a pedicle was ever present.

7. Postmortem examination of the abdomen showed one calcareous nodule on the small bowel, which was, however, entirely

covered by peritoneum, and another surrounded by adhesions in the neighborhood of the large bowel.

8. The centre of the mass was calcareous.

9. Section of the tumor showed that about this calcareous centre were concentric rings (in three dimensions), similar to those seen about the nucleus of a vesical calculus.

10. Microscopically, the tumor consists of a homogeneous tissue arranged in concentric layers, the exact nature of which cannot be determined, but which probably are either fibrin or organized fibrin, with disappearance of the cellular elements.

As to the origin of the tumor, the following explanations seem worthy of discussion.

1. The tumor may represent a pediculated fibroid or fibroma, which was originally attached to some viscus, or to the abdominal parietes, and became detached, calcified in the centre, and remained a foreign body in the peritoneal cavity. The entire absence of any sign of pedicle, not only on the surface, but in the outline of the concentric rings, vitiates this hypothesis.

2. A calcareous mass similar to those found at autopsy, or indeed a small fibroma in such a situation, might have gradually grown by having new layers added to it from the surrounding envelope of peritoneum, until reaching a certain definite size, its mere weight, or accident tears a way through the peritoneal covering, leaving it a free body in the abdominal cavity.

3. The small tumor or nodule, freed from its attachment in the above manner, may have continued to grow within the abdominal cavity, much as a pearl does in the shell of an oyster, causing a certain irritation of the peritoneum, and an outpouring of fluid and cells (there was definite fluid present). The coagulation of fibrin over the offending surface and the gradual organization of the same might follow. The definitely recurring layers are in favor of some such view.

4. A combination of the second and third is, of course, another possibility, and is perhaps the most likely. That is to say, the earliest growth took place subperitoneally or elsewhere, and the later growth, while it was a free body in the peritoneal cavity. Calcification may have occurred at any time.

We have been unable to find any report of a similar case, though it is quite possible that such may have escaped our notice, owing to the difficulty of classifying an unusual condition in the literature.

Fibromas of the abdominal parietes and contents have been noted, but are not common. The instances recorded do not seem to throw any light upon the present case.

THE VALUE OF PETECHIÆ IN DIAGNOSIS AND PROGNOSIS.

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EVERY case of doubtful diagnosis should be thoroughly inspected for evidences of hemorrhagic lesions. In the routine examination of a patient, an enlarged spleen, a cardiac murmur, or an abnormal abdominal mass are seldom overlooked; but a subconjunctival hemorrhage or a crop of petechiæ around the knee are just as seldom observed. The finding of a minute petechia on the mucous membrane of the palate or in the conjunctiva will not definitely establish a correct diagnosis, but it will, by eliminating the many conditions in which these hemorrhages are absent and by furnishing a positive sign which we cannot discard, serve as a great aid in the solution of the problem.

The idea in mind in writing this paper is not to compile an exhaustive treatise on the hemorrhagic eruptions, but to mention several unusual cases in which the occurrence of petechiæ afforded a clue to the proper diagnosis or was striking on account of its rarity in these cases. A summary in the beginning, of the common conditions in which we are likely to find petechiæ, should not be irrelevant. They are as follows:

1. ACUTE INFECTIOUS DISEASES. Any bacteriemia may develop petechiæ, as pneumonia, bacterial endocarditis, postpartum or post-traumatic sepsis, in which cases the hemorrhages may be embolic in origin. This may be likewise true in cases of pernicious malaria, many of which are accompanied by a petechial eruption; in some of these cases thrombi produced by masses of bacteria have been found in the brain at autopsy. Under the heading of acute infections we may also classify those diseases in which there is not a general systemic infection or at least in which our present laboratory methods are insufficient to establish a bacteriemia, as in yellow fever, most cases of cerebrospinal meningitis, and the acute exanthemas, as scarlet fever, measles, and smallpox.

2. TOXIC STATES NOT ASSOCIATED WITH OR SECONDARY TO BACTERIAL INFECTIOUS AGENTS. In this category as causative factors are:

(a) *Drugs*: As quinine, copaiba, belladonna, potassium iodide, alcohol, ergot, chloral, salicylic acid, and benzine vapor.

(b) *Urinary Sepsis*: In uremia or after operative procedures upon the urinary tract, where the patient is overpowered by the toxins due to a suppression or retention of urine, petechiæ are not uncommon.

(c) *Snake-bite*.

(d) *Jaundice*.

In the latter two conditions there is often a general hemorrhagic tendency evidenced not only by purpura, but in many instances by extensive subcutaneous extravasations.

3. BLOOD DISEASES. Practically all the blood diseases may show at some time a more or less extensive petechial eruption, as leukemia, pernicious anemia, etc. Under this heading, or under that of the acute infectious diseases, we may classify the simple and the so-called "rheumatic" purpuras, the Henoch's and Schönlein's type, and the "erythema group" of Osler's, in which hemorrhagic lesions are characteristic.

4. CONDITIONS PRODUCED BY MECHANICAL CAUSES. Sudden changes of atmospheric pressure, as in caisson disease, or paroxysms of coughing, as in pertussis, or convulsions of any kind, are likely to be associated with hemorrhages.

5. EXHAUSTIVE STATES. Carcinoma, tuberculosis, Hodgkin's disease, and other wasting illnesses in their last stages are known to produce petechial and other hemorrhagic lesions.

6. NERVOUS DISEASES. Both organic diseases, as myelitis and tabes dorsalis, and functional conditions, as hysteria, are occasionally associated with skin hemorrhages.

Petechiæ in bacterial endocarditis, in Henoch's purpura in epidemic cerebrospinal meningitis, and in the bacteriemias of pyogenic origin are not uncommon. I shall take occasion, therefore, to cite only unusual cases, which I observed recently while in charge of the admitting department of the Mt. Sinai Hospital, in which petechiæ played an important part in the diagnosis.

CASE I.—*History of erysipelas followed in two weeks by high fever and prostration; petechiæ in conjunctiva; diagnosis of streptococcemia made; Bacillus typhosus in blood culture.*

C. Z., aged thirty-six years. (Service of Dr. Rudisch.) The past history was negative. There were no infectious diseases. Four weeks before admission the patient had been treated for erysipelas of the leg, which had run a mild course, and had apparently been cured in about a week. For the two weeks prior to admission there had been gradually increasing headache, fever, malaise, and shortness of breath. On admission the patient appeared mildly prostrated. Evidences of the former erysipelas had entirely disappeared. The temperature was 103° and the pulse 110. In the left lower conjunctiva were three distinct petechiæ, in the right, one. The remainder of the physical examination was negative. The spleen was not felt; the pulse was not dirotic; there was no eruption. The diagnosis of bacteriemia secondary to the previous erysipelas was made. The day after admission fresh petechiæ were found in both conjunctivæ. The blood-count showed a slight leukocytosis, with 66 per cent. of polynuclear leukocytes, 33 per cent. of lymphocytes, and 1 per cent. of transitionals. The temperature ranged between 103° and 105°. Four days after

admission the spleen became palpable. The blood-culture taken the day of admission was reported positive, not for the *Streptococcus pyogenes* or *staphylococcus*, as was expected, but for the *Bacillus typhosus*. The patient became more and more prostrated. Several days after admission there were evidences of intestinal hemorrhage; a week later perforation of the bowel occurred, resulting in death, despite the early diagnosis and immediate operation.

A search of the literature fails to show many cases of typhoid fever with petechiæ on record. In fact, the one distinguishing sign which differentiated typhoid and typhus fever in the days when the latter disease flourished was the presence of petechiæ in typhus. This must be considered, therefore, as a rather unusual case.

CASE II.—*Acute onset with fever, vomiting, and convulsions, in a child; signs of meningitis; skin petechiæ; no meningococci in spinal fluid; recovery; acute polioencephalitis.*

J. B., aged five years. (Service of Dr. Koplik.) The child had been well up to four days prior to admission, at which time the patient had become acutely ill with fever and headache. He had vomited once at the onset. Just before the child was brought to the hospital he had had a general convulsion lasting ten minutes. Physical examination revealed a condition of semistupor, a temperature of 104°, a slight Macewen sign, a *tâche cérébrale*, a Babinski reflex on the right side, and a Brudzinski sign. On the skin over the right deltoid were five or six small but definite, apparently recent, petechiæ. There was no rigidity of the neck; there were no palsies. The diagnosis of epidemic cerebrospinal meningitis was made. The next day the following data were obtained: Blood-count, 18,200 white blood cells, with 85 per cent. polynuclear leukocytes and 15 per cent. lymphocytes. On lumbar puncture, 12 c.c. of clear fluid under pressure was obtained, the cytology of which was later reported to be 100 per cent. lymphocytes. No tubercle bacilli were found. Four days afterward a facial palsy became apparent, and the next day decided weakness of the right leg. The stupor was somewhat less marked, but the other signs of meningitis seemed to be on the increase. Within twenty-four hours, however, the symptoms abated, the palsies lessened, the petechiæ disappeared, and the patient steadily improved until his discharge three weeks later, at which time he had fully recovered.

That polioencephalitis and meningitis are not easily distinguishable in many cases is a matter of common knowledge. It is, therefore, rather unfortunate for the science of diagnosis that the classical sign of cerebrospinal meningitis, the sign that caused it to be known as spotted fever, and upon which the diagnosis has often been made, should be usurped by another condition so analogous in its manifestations.

CASE III.—*Acute lobar pneumonia; jaundice; pneumococcic sepsis; petechiæ.*

J. B., aged thirty-eight years. (Service of Dr. Manges.) The patient's present illness began six days before entering the hospital, with a chill, fever, and pain in the right side of the chest. Later a slight cough developed. All symptoms increased to the time of admission. The examination on admission revealed signs of a lobar pneumonia on the right side, extending almost to the spine of the scapula. The patient showed evidences of marked prostration. There was a double mitral murmur, but no signs of cardiac decompensation. Jaundice appeared soon afterward and steadily progressed. One week after admission several crops of petechiæ were observed over both shoulders. The blood-culture taken at this time showed the pneumococcus. The patient's general condition became gradually worse, and he died two days later.

In this case, although it is conceivable that the petechiæ may have been dependent upon the jaundice, it is more probable that they were due to the pneumococcemia. Petechiæ in pneumonia, even without a demonstrable bacteriemia, may occur, although these cases are not common. An analogous case, also on the service of Dr. Manges, I reported about six months ago. Here, however, the diagnosis presented some difficulty, from the fact that the petechia was in the conjunctiva and minutely resembled those characteristic of bacterial endocarditis.

CASE IV.—*Emaciation; marked anemia; conjunctival petechiæ; admitting diagnosis: pernicious anemia; blood-count typical of lymphatic leukemia.*

E. S., aged forty-six years. (Service of Dr. Brill.) This patient gave a history of a rather vague onset, two months prior to admission, of epigastric cramps and anorexia. These symptoms continued with, in addition, a steady decline in weight. Excessive thirst was the patient's chief complaint. There was no vomiting, no polyuria, no bleeding from any mucous membrane. On admission the patient looked anemic, and showed evidence of marked emaciation and asthenia. The tongue was extremely dry and rather beefy in its appearance. The liver was enlarged to two fingers below the free border of the ribs. There were no glands or spleen to be felt. The reflexes were somewhat exaggerated. In both lower conjunctivæ there were several small but definite petechiæ. There were three possibilities considered at the time of admission: diabetes, eliminated by the negative result of the urinary examination, malignancy, and a blood disease. The last diagnosis was finally decided upon, and the patient admitted to the wards with the working diagnosis of pernicious anemia, no blood-count, however, having been taken in the admitting department. On the wards the blood-count was shown to be 40,000 white blood cells; small lymphocytes, 54 per cent.; large lympho-

cytes, 44 per cent.; polynuclear leukocytes, 2 per cent.; and hemoglobin, 42 per cent. Three days afterward petechiæ were seen on both arms. Later, diarrhea and weakness became marked, the skin hemorrhages increased greatly in number, and the patient finally died about three weeks after admission. At no time were there glands or a spleen to be felt.

In this case, although, of course, the petechiæ did not determine the diagnosis, they were, taken together with the anemia, instrumental in limiting the diagnosis to that of a blood disease. The exact type of blood disease was of secondary importance at the original examination. In several other cases of leukemia seen recently the diagnosis was suggested by the presence of skin and subconjunctival petechiæ, enlarged glands, and a palpable spleen having been absent.

CASE V.—*Signs of purpura hemorrhagica; steady progression of symptoms; ulcerations and gangrene; fatal outcome.*

H. A., aged fourteen years. (Service of Dr. Manges.) The past history was negative, with the exception of frequent attacks of tonsillitis. Six weeks before her appearance at the hospital, after exposure, the patient felt chilly, and complained of general aching pains and a soreness and redness of the left eye. These symptoms abated in a few days, but recurred five weeks later, accompanied by pain in the right wrist and knee. The day before admission the swelling of the right wrist and knee became aggravated, and was accompanied by a chill, considerable fever, and the appearance of a moderate number of small red spots in the skin around the swollen joints. On admission the patient looked acutely ill and in severe pain. Both wrists, ankles, and knees were swollen, red, and tender to the touch. Around several of the joints, in the conjunctivæ, and on the abdomen, were petechiæ, some minute, others as large as the head of a pin; on the buttocks were two somewhat larger hemorrhagic areas. The subsequent course of this patient presented a picture never to be forgotten. Daily, almost hourly, fresh hemorrhages occurred on the chest, abdomen, legs, buttocks, and in the mouth. All of these steadily underwent the same transformation. The hemorrhages would increase in size to that of a ten-cent piece or even a quarter, then develop around their periphery an inflammatory red zone, begin to ulcerate, become foul-smelling, gangrenous, and finally slough away. Despite all methods of treatment this process of destruction continued to increase, until just before death one-third of the skin of the body and of the mucous membranes of the mouth, larynx, rectum, and vulva was involved. The patient died three weeks after admission.

This case has been reported on account of its rarity. The simple purpuras, the rheumatic purpuras, and those associated with visceral manifestations usually have an excellent prognosis. It

is uncommon to see a case of this description, manifestly rheumatic in etiology, resist all therapeutic measures and terminate fatally.

CASE VI.—*Case of myocarditis and nephritis; Bacillus coli communis pyelitis; petechia in conjunctiva; sudden death.*

G. B., aged forty-nine years. (Service of Dr. Rudisch.) The patient gave the usual history of a cardionephritic case; dyspnea, slight edema of the legs, and cough for many months. Several days before admission the swelling of the legs had increased considerably, and the urine had become scanty. There had been slight fever and occasional sweats; no chills. Examination revealed the clinical signs of myocarditis, with nephritis, dyspnea, pulmonary congestion, weak heart sounds, swollen liver, and edematous legs. Besides this, there was found in the left lower conjunctiva a distinct petechia. The urine showed considerable albumin, pus, red blood cells, and many casts. Culture of a catheterized specimen showed the *Bacillus coli communis*. The petechia disappeared within forty-eight hours. The patient gradually improved and had been out of bed for several days, when he was suddenly seized with a convulsion, followed by almost immediate death.

Similar cases are not uncommon. One analogous case was seen recently on the service of Dr. Brill, where the lower extremities of a nephritic patient were almost covered with minute petechiæ. It is conceivable that these small hemorrhages may be the result of increased blood-pressure or may be evidences of a toxemia. In favor of the latter theory may be mentioned instances of petechiæ in those cases of so-called urinary sepsis following kidney or prostate operations, where the system is poisoned by an accumulation of toxins unable to be eliminated by the usual channel.

CASE VII.—*History of a debauch; conjunctivitis; numerous petechiæ in upper and lower conjunctivæ.*

A. B., aged twenty-seven years. This patient was seen twelve hours after a night of dissipation. He was unaccustomed to the frequent use of intoxicating liquors. Six months before, a similar debauch was followed by the same symptoms. There was evidence of a mild conjunctivitis. In the upper and lower conjunctivæ of both eyes were seen many petechiæ of varying sizes, not merely dilated bloodvessels, but actual hemorrhages into the tissues. Seventy-two hours elapsed before the absorption of these hemorrhages.

It is interesting to note that the toxic effect of the alcohol in this case was, so far as could be observed, confined to the bloodvessels of the conjunctiva, the vessels of all other mucous membranes and the skin apparently having been spared. In all probability, however, the upper gastro-intestinal tract was likewise studded with minute hemorrhages, the result of the poison upon a delicate membrane; but of this we have no proof.

CASE VIII.—*History suggestive of an acute exacerbation of a chronic nephritis; marked eosinophilia; conjunctival petechiæ; trichiniasis.*

M. R., aged twenty-two years. (Service of Dr. Rudisch.) With the exception of indefinite pains in both loins and occasional urinary disturbances, the past history of this patient had been negative. Three weeks before admission the patient had complained of the symptoms of an influenzal infection; headache, fever, chilly sensations, and general body pains. The fever had subsided after a few days and had not recurred. The urine had been somewhat scanty, the face had become swollen, and the headache had continued. There had been some vomiting. At the time of the original examination the patient appeared to be suffering from nephritis, as evidenced by the puffy face and eyelids and the history of scanty urine, headache, and vomiting. The urine showed a heavy trace of albumin, but no casts. In the lower left conjunctiva were many small petechiæ. Distinct tenderness was elicited over the deltoid muscles and those of the calves. There was no fever. The blood-count was reported to be 12,600 white blood cells, of which there were 62.5 per cent. of polynuclear leukocytes, 19 per cent. of lymphocytes, and 18.5 per cent. of eosinophiles. Subsequent blood examinations revealed the presence of eosinophiles in even larger proportions, the highest count showing 37 per cent. The hemorrhages disappeared within a few days. The stools contained no ova or parasites of any kind. The diagnosis of trichiniasis was made, although the trichinæ were not demonstrated.

Petechiæ in this disease are uncommon, and so could not have been of any great assistance here in determining the diagnosis. This case is interesting, however, and illustrates the wisdom of looking for hemorrhages where trichiniasis is suspected.

CASE IX.—*History of bite by rabid dog; increasing irritability, finally coma and death; skin petechiæ.*

H. S., aged nine years. (Service of Dr. Koplik.) Twenty-six days before admission this patient had been bitten on the face by a dog. The next day both patient and dog were taken to the Pasteur Institute, where the dog was killed and proved to have had rabies. The child had then undergone eighteen treatments at the institute, and had been discharged about ten days before admission to Mt. Sinai Hospital, apparently cured. Three days afterward he had suffered an attack of prolonged vomiting. Since then there had been increasing restlessness, irritability, delirium, and finally, the day before admission, coma. In addition the parents had noticed for two days a peculiar twitching of one side of the mouth for several minutes at a time. There had been no convulsions, no photophobia, no history of the refusal of water. The physical examination revealed a child in coma, absolutely unresponsive, with slight spasticity of the lower extremities, a MacEwen sign, and an occasional clonic twitching of one side of the face, especially at the angle of the mouth. Over the chest, the

lower abdomen, the shoulders, and in the folds of the elbow were many small but unmistakable petechiæ. There was no neck rigidity, no Kernig, no Babinski sign, no tâche cérébrale. The temperature was 104°. On lumbar puncture, 20 c.c. of faintly turbid fluid under slightly increased pressure was obtained. The bacteriology of the fluid was negative; there were no meningococci, no tubercle bacilli. Of the cells seen, 90 per cent. were lymphocytes, 10 per cent. polynuclear leukocytes. The child's condition steadily grew worse, and he died fifteen hours after admission.

In the diagnosis of this case, petechiæ were valueless. Without the previous history of a dog-bite, the diagnosis of rabies, which this in all probability was, though no necropsy was obtainable, would have been impossible, the acute onset, the previous irritability, the coma, and the petechiæ especially, indicating an epidemic cerebrospinal meningitis. This case is reported merely as another example of the occurrence in children of a hemorrhagic eruption in conditions resembling "spotted fever."

CASE X.—*History and signs of acute appendicitis; chills and fever; petechiæ in conjunctivæ; weak heart sounds; diagnosis of bacterial endocarditis with mesenteric embolus; acute gangrenous appendicitis found at operation.*

D. C., aged twenty-nine years. (Service of Dr. Lilienthal.) The history had been negative, with the exception of an attack of somewhat similar nature, although not so severe about four months previous to admission. Five days before admission the patient had complained of headache, mild epigastric pain, and general weakness, had gone to bed, and had apparently improved for two days, when he had suddenly vomited and complained of severe pain in the right iliac region, accompanied by fever and chilly sensations. The last three symptoms had continued to date. There was no history of hematemesis or melena. The physical examination was extremely interesting. The patient looked acutely ill. The temperature was 102°. On account of the abdominal symptoms, the abdomen was first examined. Marked tenderness over the entire right lower quadrant, some rigidity, less tenderness over the remainder of the abdomen, and the suggestion of movable flatness pointed to the diagnosis of appendicitis. In doing the remainder of the physical examination in a routine way, four distinct petechiæ were discovered in the right and three in the left conjunctiva. The heart sounds were found to be extremely weak, but there was no evidence of an endocardial murmur. Despite this, the diagnosis of bacterial endocarditis with a mesenteric embolus was hazarded, the possibility of an acute gangrenous appendicitis, however, having been kept in mind and the surgical indication recognized. The patient was operated upon immediately and a gangrenous appendix with spreading peritonitis found. The patient made an uninterrupted recovery, and was

discharged in about two and a half weeks after his operation. The petechiæ disappeared in seventy-two hours after admission.

The etiology of the petechiæ here is a matter of conjecture. That they were manifestations of a bacteriemia secondary to a diseased appendix can hardly be considered, inasmuch as appendicitis is practically never followed by a general systemic infection, pyelphlebitis and multiple liver abscesses without a bacteriemia being the usual sequelæ of a fulminating or a neglected case. Infective endocarditis may be eliminated by the disappearance of the petechiæ, the absence of a cardiac murmur, and the speedy recovery of the patient. We must be satisfied with the explanation that although the patient did not appear much prostrated, the toxemia nevertheless must have been sufficiently intense to have produced the conjunctival hemorrhages. A similar case was seen and operated upon several years ago by Dr. Elsberg, by whose kind permission I am citing the case. Here there had been a history, dating back several days, of abdominal pain and gastric distress, together with joint pains and a petechial eruption around the joints. There were petechiæ in the conjunctivæ. It was difficult to decide between a gangrenous appendicitis and "visceral crises of the erythema group." Prompt operation revealed the former condition. Here a culture of the sticky pus around the appendix was taken and reported to contain the *proteus vulgaris*.

Besides their importance in diagnosis, petechiæ may be considered to have some value in prognosis. In these days, when so much work is being done upon endocarditis accompanied by bacteriemia, one is prone to look with suspicion upon every case of endocarditis with petechiæ. Such a suspicion is justifiable, of course, but one must bear in mind the possibility, as evidenced by the foregoing examples, of other causes of petechiæ; so that what is most important to the patient, the prognosis, should not be definitely stated until bacteriological methods have confirmed the diagnosis. In children under ten years of age I have seen several cases of endocarditis, and one case of endopericarditis, with fever, chills, conjunctival and palatal petechiæ, which were clinically cases of bacterial endocarditis, give a negative blood culture, and so far as their acute symptoms are concerned, become entirely well. In other infectious diseases, as in typhoid fever, pneumonia, and the acute exanthemas, the presence of petechiæ renders the prognosis serious but not necessarily fatal. Where these hemorrhages are present, the case is often a fulminating one. Likewise in chronic nephritis and in other conditions of renal origin, petechiæ indicate extreme toxemia. The few cases reported will serve, I trust, to prove the value of petechiæ in diagnosis and prognosis, and to encourage the physician to hunt for them in the skin, in the mouth, and in both upper and lower conjunctivæ, in any questionable case.

THE NEUTROPHILIC BLOOD PICTURE IN PERNICIOUS ANEMIA: A PRELIMINARY REPORT.

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IN the course of some work on the Arneth blood picture in various conditions, the multiplicity of lobes of the neutrophiles in a case of pernicious anemia was observed. This particular point has since been studied in nine consecutive cases seen during the past year and in the stained smears from three others. The rather striking results found, together with the lack of mention of this feature in the text-books and monographs in general use, have prompted the publication of a preliminary report in order that further observations by others may be recorded.

So far as could be ascertained in a search of the literature, the only mention of similar findings were two. v. Decastello,¹ reporting a case of splenectomy for pernicious anemia, in speaking of the blood picture, noted the abnormal number of nuclei of the neutrophiles, "abnormen Kernpolymorphismus." Brosamlen,² in a discussion of the blood in pernicious anemia during remissions, stated that an Arneth shift to the right was present in all cases (seven), but gave no figures. All the standard text-books dismissed the neutrophiles in pernicious anemia with the statement that they were, as a rule, diminished, both relatively and absolutely.

In the present note attention is called to the fact that in ten out of twelve cases a decided increase in the normal number of lobes of the nuclei of the neutrophiles was found, *i. e.*, a "shift to the right" in the terms of Arneth. It is further shown for comparison that in eight cases of correspondingly severe anemia, not of the idiopathic pernicious variety, seven showed either a normal number, or a decrease in the number of lobes, a "shift to the left."

There is no intention of entering here into a discussion of the value of the Arneth count. In this work it has been utilized simply as a convenient method for the study and classification of the neutrophiles. As is well known, the neutrophiles can be divided into five classes according to the number of separate lobes of their nuclei. The classical formula of Arneth was 5 per cent. in the first class, 35 per cent. in the second, 41 per cent. in the third, 17 per cent. in the fourth, and 2 per cent. in the fifth. The majority of workers have reported formulæ approximating this, it being

¹ Splenektomie bei perniziöser Anämie, Wien. med. Woch., 1913, xxvi, 951.

² Ueber die Bedeutung der Megalocyten bildung und über die Blutbefunde in den Remissionsstadien der perniziösen Anämie, Deutsch. Arch. f. klin. Med., 1913, cxii, 83.

found remarkably constant in normal bloods. "Shifting to the left," or an increase in the lower classes at the expense of the higher, has been regularly found in most infections and in many other pathological conditions. "Shifting to the right," the opposite of this, although noticed occasionally, has not been considered characteristic of any particular condition.

In the present series the technique used in counting has been uniform and was given in detail in a former paper.³ Differential counts were made on the basis of 500 leukocytes and nuclear counts on the basis of 200 neutrophils. The five chief classes of the original Arneth were adhered to with the "index" as the sum of the first, second, and one-half the third classes, a figure arbitrarily adopted as an easy means of comparison. Nuclei connected by anything more than the finest thread were counted as single. Nuclei plainly superimposed upon another were classed separately, and where doubt existed the cell was not tabulated.

The cases were from the medical service of the University of California Hospital and the private practice of Doctor Herbert C. Moffitt. Patients' histories are not given, but of the cases in Table I the diagnosis was made in each of idiopathic pernicious anemia of Biermer, both from a clinical and a hematological standpoint. In Table II the clinical diagnosis is given. For the sake of brevity descriptions of the red cells are omitted. In all the pernicious anemia cases, however, they exhibited the characteristic changes to greater or less degree, *i. e.*, increase in average diameter, high color, alterations in shape and size, and abnormal variations in staining reaction. In the other cases the diameter was normal or less than normal, central pallor was marked, and the various other pathological changes were less noticeable.

Discussing briefly the findings shown in Table I, it will be noted that Cases 1, 3, 5, 6, 7, 9, 10, 11, and 12 present distinctly abnormal neutrophilic pictures, in that at least three-fourths of the cells have three or more pieces to the nucleus. It may be remarked parenthetically that class five contains those cells having five or more lobes, and not infrequently nuclei may be seen having as many as eight separate pieces. Cases 2 and 8 show normal formulae. The first observation on Case 4 shows a shifting to the right, but the two subsequent examinations show counts which come just within the normal range. The severity of the case has apparently no bearing on the degree of shifting, Cases 4 (at the time of the first observation), 6, and 9 being the gravest of the series. Case 7 was in excellent condition, yet showed a tremendous alteration in his picture. Seemingly against this statement is the fact that in Cases 4 and 10, as the general condition improved, the neutrophils approached the normal, and in Cases 5, 6, and 9, as the

³ Le Roy H. Briggs, The Clinical Value of the Arneth Method of Blood Examination, California State Jour. Med., 1912, x, 337.

TABLE I.—PERNICIOUS ANEMIA.

Case number.	Date.	Hemo- globin. (Dare) per cent.	Red blood cells. per cumm.	Normo- blasts, per cumm.	Leuko- cytes. per cent.	Neutro- phils, per cent.	Large mono- nuclears and transitionals, per cent.	Lympho- cytes, per cent.	Eosino- phils, per cent.	Baso- phils, per cent.	Myelo- cytes per cent.	Class I.	Class II.	Class III.	Class IV.	Class V.	Index.
Case 1, J. R. S.	April 1, 1909	38	1,609,000	Few	2,800	62.8	2.8	31.2	3.2	0	0	0	20.0	35.0	34.0	11.0	37.5
Case 2 U. C. H., No. 2752	Sept. 26, 1910	40	2,202,000	Few	4,800	71.4	4.0	21.6	3.0	0	0	2.5	27.0	43.5	22.5	5.0	51.25
Case 3, Li.	Sept. 11, 1912	45	1,968,000	0	6,000	74.0	3.8	20.6	1.2	0.4	0	2.5	16.0	42.0	28.5	11.0	39.5
Case 4 U. C. H., No. 5298	Feb. 18, 1913	10	510,000	700	2,100	56.6	6.6	36.6	0.2	0	0	2.0	13.0	40.5	34.5	10.0	35.25
	April 8, 1913	45	2,372,000	0	5,000	50.0	8.0	37.4	4.6	0	0	3.5	25.0	45.5	18.0	8.0	51.25
	Oct. 15, 1913	55	2,872,000	0	7,000	51.6	12.0	30.4	5.6	0.2	0	5.5	25.0	39.0	25.5	5.0	50.0
Case 5 U. C. H., No. 5550	April 15, 1913	45	2,228,000	0	4,000	65.6	5.6	26.8	1.6	0.4	0	0	16.0	49.5	28.0	6.5	40.75
	May 5, 1913	50	2,996,000	0	4,200	57.2	8.4	30.0	4.0	0.4	0	0.5	22.5	51.0	21.0	5.0	48.5
	Dec. 20, 1913	40	2,406,000	Few	5,400	53.4	12.8	27.8	5.8	0.2	0	0	19.5	47.0	20.5	14.0	33.0
	Jan. 7, 1914	35	2,841,000	0	7,100	66.6	9.4	22.0	1.8	0.2	0	0	13.0	42.5	34.0	10.5	34.25
Case 6 U. C. H., No. 5582	April 28, 1913	15	1,078,000	400	2,800	59.0	7.0	31.6	2.4	0	0	3.0	17.5	39.5	29.0	11.0	40.25
	May 5, 1913	20	963,000	1600	4,800	73.8	2.4	21.0	2.2	0.4	0.2	2.0	10.5	42.5	26.0	19.0	33.75
Case 7, Ha.	May 26, 1913	60	2,504,000	0	9,300	64.4	4.4	26.2	5.0	0	0	0	4.5	24.0	38.5	33.0	16.5
Case 8 U. C. H., No. 6279	Oct. 8, 1913	55	2,960,000	Few	8,100	61.0	12.2	24.0	2.6	0.2	0	3.5	36.5	44.0	15.0	1.0	62.0
	Dec. 9, 1913	70	4,920,000	0	5,900	53.4	10.4	31.0	4.2	1.0	0	4.0	30.0	50.0	14.5	1.5	59.0
	Feb. 27, 1913	80	5,672,000	0	7,200	48.6	11.0	38.8	0.8	0.8	0	1.0	22.0	49.0	22.5	4.0	48.25
Case 9, Hf.	Dec. 4, 1913	25	955,000	500	5,100	62.6	2.6	33.0	0	0.2	1.6	6.0	17.5	35.0	25.0	16.5	41.0
	Dec. 12, 1913	20	736,000	400	7,000	72.0	1.4	25.6	0	0.2	0.8	2.0	11.0	30.5	31.0	25.5	28.25
Case 10 U. C. H., No. 6598	Dec. 19, 1913	35	2,172,000	Rare	5,100	80.6	5.8	13.4	0.2	0	0	0.5	15.0	29.0	32.0	23.5	30.0
	Jan. 16, 1914	55	3,100,000	0	6,600	57.2	11.8	28.2	1.8	1.0	0	1.0	17.5	41.5	27.0	13.0	39.25
	Feb. 10, 1914	60	3,904,000	0	5,100	48.2	7.6	39.4	3.6	1.2	0	1.0	20.5	45.5	26.5	6.5	44.25
Case 11, Gn.	Jan. 3, 1914	40	1,500,000	Few	5,000	65.4	4.0	26.4	3.6	0.2	0.4	1.5	10.5	28.5	34.0	25.5	26.25
Case 12, Hu.	Feb. 27, 1914	50	2,146,000	Few	7,200	61.2	3.8	33.6	1.0	0.2	0.2	1.5	16.0	38.5	31.5	12.5	36.75

TABLE II.—SECONDARY ANEMIA.

Case number.	Diagnosis.	Date.	Hemo- globin. (Dare) per cent.	Red blood cells.	Normo- blasts per c.mm.	Leuko- cytes.	Neutro- phils, per cent.	Large mono- nuclears and transitionals per cent.	Lympho- cytes, per cent.	Eosino- phils, per cent.	Baso- phils, per cent.	Myc- elocytes, per cent.	Neutrophiles.					Index.
													Class I.	Class II.	Class III.	Class IV.	Class V.	
Case 1 Pa.	Sarcoma of tongue.	Jan. 16, 1913	35	2,260,000	0	8,300	67.0	8.8	24.0	0	0.2	0	13.0	54.0	32.5	0.5	0	83.25
Case 2 U. C. H., No. 5309	Nephritis, syphilis, terminal pericar- ditis.	Feb. 20, 1913	15	1,800,000	0	14,400	79.6	3.6	10.8	4.6	1.4	0	3.5	37.0	43.0	15.0	1.5	62.0
		Feb. 25, 1913			Few		84.6	7.4	6.2	1.4	0.4	0	8.5	45.0	40.0	6.5	0	73.5
Case 3 U. C. H., No. 5838	Possible Banti.	June 28, 1913	50	3,120,000	0	5,100	65.8	8.8	18.4	6.6	0.4	0	18.0	57.5	22.5	2.0	0	87.25
		Sept. 24, 1913	60	3,720,000	0	6,200	58.8	7.0	16.4	16.4	1.4	0	16.0	59.0	24.5	0.5	0	87.25
Case 4 U. C. H., No. 5848	Syphilis	June 28, 1913	38	3,000,000	Rare	9,700	65.4	6.2	28.4	0	0	0	2.5	13.0	47.0	26.5	11.0	39.0
Case 5 U. C. H., No. 5828	Duodenal ulcer with hemorrhage	June 28, 1913	20	2,064,000	0	9,900	69.0	15.0	15.8	0	0.2	0	7.0	38.0	40.5	11.5	3.0	65.25
Case 6 U. C. H., No. 5944	Cirrhosis of liver with hemorrhages	July 20, 1913	18	1,516,000	Rare	14,400	73.6	4.2	21.8	0.4	0	0	2.5	35.0	41.0	18.5	3.5	58.0
Case 7 U. C. H., No. 6379	Chronic lymphatic leukemia	Oct. 24, 1913	35	2,550,000	Many	225,000	2.0	1.0	97.0	0	0	0	19.5	43.5	25.5	7.5	4.0	75.75
Case 8 U. C. H., No. 6485	Probable malignancy of intestine.	Nov. 17, 1913	10	1,800,000	0	11,900	64.2	14.3	17.9	2.7	0.4	0.3	4.5	40.5	43.0	10.5	1.0	66.5
		Dec. 10, 1913	10	2,400,000	0	11,800	72.0	9.2	13.4	4.4	1.0	0	3.0	31.0	52.5	10.5	3.0	60.25
		Jan. 15, 1914	18	2,312,000	250	14,200	75.8	10.8	10.8	2.2	0.4	0	2.5	36.5	43.5	16.0	1.5	60.75

general condition grew worse, the shifting to the right became more marked. Case 8, an early case which improved greatly, however, presented normal formulæ at two observations and a very slight shifting to the right at a third.

Table II is inserted simply for comparison as showing eight consecutive cases of approximately similar grades of anemia, not, however, of the idiopathic type. Only one of these, Case 4, shows a shifting to the right. The anemia in this case was beyond question a secondary one, but further observations were unfortunately not made. Cases 5 and 6, both anemias of rapid onset, showed normal neutrophilic pictures. Case 2 at the first examination and Case 8 throughout also showed normal formulæ, although the former died the day following the second count, and the latter was in very bad condition. The others showed a moderate degree of shifting to the left, a not unexpected finding.

Nothing further can be said in this note. Its purpose is simply to call attention to the increased number of nuclear particles of the neutrophiles in pernicious anemia, a point doubtless noticed many times before, but evidently worthy of further study.

REVIEWS

DISEASES OF THE SKIN. BY GEORGE THOMAS JACKSON, M.D., Late Professor of Dermatology, College of Physicians and Surgeons, New York; Consulting Dermatologist to the New York Infirmary for Women and Children; Member of the American Dermatological Association and New York Dermatological Society, etc. Seventh edition; 770 pages; 115 illustrations; 6 plates. New York and Philadelphia: Lea and Febiger, 1914.

DR. JACKSON'S admirable, compact little volume has been thoroughly revised and a considerable number of new illustrations added. The book is alphabetically arranged so as to be a ready reference hand-book for the student and general practitioner. Thirty-two pages have been added to the last edition to bring the present work up to date. New sections have been added on acarodermatitis, cutis verticis gyrata, eczema marginatum, eczematoid dermatitis, erythema figuratum perstans, gangosa, granuloma coccidioides, ground itch, hemisporosis, keratoderma gonorrhoeica, leukema cutis, lichenification, lichen nitidus, lichen planus sclerosus et atrophicus, and trypanosomiasis. Several of the old sections have been rewritten.

The work is made of greater value by articles on vaccine treatment, written by Dr. M. F. Engman; on the administration of salvarsan, contributed by Dr. John A. Fordyce; and on Roentgen therapy, compiled by Dr. G. M. MacKee. An admirable photomicrograph of the *Spirocheta pallida*; a water-color painting of sporotrichosis, and several excellent practical clinical photographs have been supplied to the present volume by Drs. H. Noguchi, Howard Fox, and Arndt.

The twelve-page appendix, filled with well-known and time-honored prescriptions, is a valuable addition to the work. There is much to commend and very little to criticise in Dr. Jackson's book, which has been so successful. There has to be a certain amount of repetition in an alphabetically arranged work on dermatology. As the pages are rather small some of the photographs are not shown to their greatest advantage. A few of the illustrations are not of the excellence of the others and might be omitted.

F. C. K.

DIE UNTERSUCHUNG DER LUFTWEGE. Ein Vortrag zur Einführung in die moderne Rhino-laryngologie für Aerzte und Studierende. By DR. P. H. GERBER, A. O. Professor und Direktor der Königlichcn Universitäts-Poliklinik für Hals und Nasen-krankc zu Königsberg I. Pr. Pp. 49; 61 illustrations. Wurtzburg: Verlag von Curt Kabitzsch.

IN his introduction Professor Gerber states that he has prepared this pamphlet, for in size at least, it is only that, with the help of his assistant Dr. Schlesinger, and Dr. Greene of New York, in order to broaden the knowledge of the profession in general as to the principles of the modern methods used in the examination of the upper and lower air passages. It seems to the reviewer that this idea is perfectly sound and that this little work would not be out of place in the hands of every practitioner in the least interested in the diagnosis of pathological conditions of the upper respiratory tract. Like most modern German works on the nose and throat the illustrations are excellent; and also like many of them the text is simply explanatory of the illustrations. The terse, brief descriptions do not give sufficient detail of the different technics to warrant anyone attempting, for instance, such procedures as bronchoscopy. The book is devoted entirely to technic and is a good illustration of the advances made in the last few years in the methods employed in the examination of the air passages, and which have revolutionized the whole practice of rhino-laryngology.

G. M. C.

MICROBES AND TOXINS. By Dr. ETIENNE BURNET, of the Pasteur Institute, with a preface by ELIE METCHNIKOFF, translated from the French by DR. CHARLES BROQUET and W. M. SCOTT, M.D. Pp. 316; 70 illustrations. New York and London: G. P. Putnam's Sons.

THIS admirable book presents to the medical man or biologist, indeed to the interested and intelligent layman, a complete review of the present day conception of microbiology, more particularly from the French standpoint. It is not a morphological treatise, but an analysis of the normal and pathological physiology of microscopic plants and animals. The first part is devoted to a exposition of the interdependence of the plant and animal kingdoms, with a thorough analysis of the fermentations and putrefactions necessary for continuation of life upon this planet. From this the author proceeds to a consideration of commensal and parasitic symbiosis, from which it is but a step to the discussion of microbes as disease producers. A large part of the book is

devoted to the various phases of immunity. The text ends with chapters on bacterial and chemical therapy.

The book is written in a clear, easily readable, convincing style. It is admirably translated. Prof. Metchnikoff has written the introduction tracing the history of microbiology and indicating that at his suggestion Dr. Burnet was asked to prepare the work. A glossary and index are included. H. F.

HEALTH AND LONGEVITY THROUGH RATIONAL DIET. By ARNOLD LORAND, M.D., Carlsbad. Pp. 416, Philadelphia: F. A. Davis Co.

THIS volume is intended to meet the popular demand for reliable scientific information of the subject of nutrition and diet. The general principles of nutrition are laid down clearly and impartially, without too much detail. The advantages and disadvantages of all the more important foods are discussed in the light of these principles and of the author's extensive experience and observation. The book is a readable one but the physician need not look to it for new or original points of view. It is, however, as Vaughan states in the introduction, "free from the facts which render so many of the books written on this subject for the laity harmful."

C. B. F.

DISEASES OF THE EYES. By C. DEVEREUX MARSHALL, F.R.C.S., Surgeon to the Royal London (Moorfields) Ophthalmic Hospital, and Ophthalmic Surgeon to the Victoria Hospital for Children, Chelsea. Pp. 303; fully illustrated. London: University of London Press, Hodder & Stoughton and Henry Frowde.

LIKE other manuals of its kind this book gives a *resume* of the present state of ophthalmic science and practice. It is not much better nor worse than the ordinary abbreviation of which there is no lack in the domain of ophthalmology. T. B. S.

THE PSYCHOLOGY OF INSANITY. By BERNARD HART, M.D., (Lond.), Lecturer in Psychiatry, University College Hospital Medical School. Pp. 173. New York: G. P. Putnam's Sons.

IN this small volume the author discusses the history of insanity, its psychological conception, the phenomena of insanity, dissoci-

ation, etc. In other words, he attempts to present the so-called modern advances of insanity in a popular edition. For the study of insanity the book is of no value because it is hardly an introduction. For the layman it is worse than useless, for the layman could hardly appreciate what is being written. It seems therefore a pity that such an important subject as psychology of insanity should be presented in this manner. T. H. W.

FREUD'S THEORIES OF THE NEUROSES. By EDUARD HITSCHMANN, of Vienna. Authorized Translation by DR. C. R. PAYNE. Pp. 154. New York: Journal of Nervous and Mental Disease Publishing Company.

WHETHER one believes or not in any new philosophy, it is always of the utmost value to have a clear and authoritative presentation of the subject. So far in the English language we have had one textbook and numerous papers, none of which have given a clear and consecutive exposition of Freud's theories. This book, therefore, which was written by one of the ablest and sanest medical men in Vienna should be welcomed. Not only has the author the opportunity of knowing Freud's theories from Freud himself but he has practised them and in this book we have for the first time a clear presentation of Freudian doctrines presented in a readable and sane manner. T. H. W.

ANAPHYLAXIS. By CHARLES RICHET, Professor in the Faculty of Medicine, Paris. Translated by J. MURRAY BLIGH, M.D., Medical Registrar to the Liverpool Royal Infirmary. Preface by T. R. BRADSHAW, B.A., M.D., F.R.C.P., Senior Physician to the Liverpool Royal Infirmary. Pp. 266. Liverpool: The University Press, London: Constable & Co., Ltd.

THE progress of recent years in the study of anaphylaxis has been so rapid that only those in a position to follow most closely the scientific literature have been able to keep themselves in touch with the knowledge concerning this important group of phenomena. The significance of this condition, however, for general medicine is very great, not only because it may possibly explain certain otherwise obscure ailments, but also because of the increasing use of certain animal proteins for subcutaneous or intravenous injection as curative measures with the possibility of producing anaphylaxis. This book gives a clear, interesting, and very readable

account of our knowledge of anaphylaxis. It opens with a brief historical sketch including five pages in which are tersely summarized the important facts known at the present time with the names of their respective discoverers and dates of publication. Then follows a detailed discussion of the incubation period, duration and symptoms of anaphylaxis, the nature of anaphylactizing substances, passive anaphylaxis, anaphylaxis *in vitro*, the relation of anaphylaxis to precipitin formation and complement deviation, anti-anaphylaxis, the relation of anaphylaxis to general medicine and a final short chapter in which the authors' theory as to the nature and purpose of anaphylaxis is outlined. This book is a most valuable one for the large number of physicians who may wish to familiarize themselves with this important subject.

J. H. A.

THE HISTORY OF PRISON PSYCHOSES. BY DRS. PAUL NITSCHKE and KARL WILMANN. Translated by FRANCIS M. BARNES, JR., M.D., and BERNARD GLUECK, M.D. Pp. 84. New York: The Journal of Nervous and Mental Disease Publishing Company.

THIS monograph is the thirteenth of the series issued by the Journal of Nervous and Mental Diseases. It is upon the important subject of prison psychoses. Of all sociological problems none are more important to the public and especially to the medical and legal professions than the study of our criminals or "near criminals." Especially is this true in the present excellent trend of the modern Juvenile Court. The present volume gives a historical review of the different viewpoints of prison psychoses so far as the German literature is concerned. It begins with an excellent introduction by William A. White.

This book should be in the hands of most medical men and all attorneys who are in the slightest way brought in contact with those who are unfortunate enough to come under the hands of the law.

T. H. W.

THE PRACTICE OF UROLOGY. BY CHARLES H. CHETWOOD, M.D., LL.D., Professor of Genito-urinary Surgery, New York Polyclinic Hospital. Pp. 816; 6 colored plates and 310 text illustrations. New York: William Wood & Co.

THE author has presented in this volume the latest and best of the thought and practice of genito-urinary surgery. The book is one of the best, if not the best single volume treatise, on the

subject of *urology*, that has appeared to date. The style of presentation is forceful, concise and well-systematized.

The book should prove not only interesting to the average physician, but unexcelled in value for the instruction of the undergraduate students in medicine. A noteworthy feature of the work is the heavy-faced printing of especially important statements throughout the book. Both author and publisher deserve professional congratulations for the general excellence and thoroughness of their respective parts.

Any remarks which are offered may be regarded, perhaps, in the light of difference of personal opinion, rather than a sustained opinion of the majority.

We do not believe that consensus of opinion will confirm the statement that the *Treponema pallidum* has not been found in the erroneously and so-called parasymphilitic diseases. Nor do we agree that the Wassermann reaction is not available until about six weeks after the first appearance of the chancre.

The chapter on "Sero-diagnosis and Sero-therapy" is commendable, but inadequate, especially that part devoted to a consideration of the gonococcus complement fixation test. Again, with respect to bacterins (vaccines), it is a mistake to advise "injections subcutaneously in gradually increasing dose at intervals of three or more days."

Photographic cystoscopy seems to be of little genuine value for the exact portrayal of intravesical appearances, and certainly there is little reason for the exhibition of Luy's separator in a work on up-to-date urology.

It is doubtful if the majority of urologists have ever observed benefit from the use of methylene blue in the treatment of gonorrhea or cystitis, or would sanction the employment of a catheter "always" in irrigating the posterior urethra in acute urethritis.

As a whole the work is very commendable, and the chapter on contracture of the neck of the bladder is a masterpiece by the man who above all others has perfected the operation most useful for its treatment.

B. A. T.

HANDBUCH DER HYGIENE. BY PROFESSORS M. V. RUBNER, M. GRUBER, and M. FISHER. Leipzig: S. Hirzel.

VOL. III, Part 3, of this Handbuch treats of the pathogenic animal parasites (protozoa, worms, and arthropods) and contains 192 illustrations in the text and 32 colored plates. The book consists of an introduction to general parasitology by Th. von Wasmann; a chapter on parasitic protozoa by Wasmann; a

chapter on parasitic worms by Wasielewski and G. Wülker; and a chapter on parasitic arthropods by W. von Schuckmann.

The diseases produced by the various parasites are indicated briefly in each case. The modes of infection are given in considerable detail and the intermediary hosts of the different parasites are enumerated. The prophylactic measures are emphasized, especially the methods of campaigns against the intermediary hosts carrying the parasites.

The control of the animal parasites is a culture problem, which, unconsciously, for thousands of years has affected all civilized people. The draining of the Campagna by the ancient Etruscans protected against malaria; the prohibition of the use of raw flesh and fish protects civilized people against the danger of infection by worms; but only the knowledge of construction, life, and mode of transmission of these parasites has pointed the way to accomplish this.

The presence of the protozoa is manifested in their influence on the host by (a) the number of parasites present, (b) the place where they are localized, and (c) the nature of their metabolic products.

In each chapter there is a brief discussion of the history of our knowledge of the different groups of parasites, followed by a description of their form and size, construction, life-activities, nutrition, division, multiplication, acquirement of parasitic functions, movements, action on the cells of the host, modes of dissemination, the insect hosts concerned in the maturation and dissemination of the parasites.

At the end of each chapter is given a list of all the important books and papers bearing on the subject. This volume is up-to-date in every respect and is a valuable contribution of this important branch of the broad subject of hygiene. D. H. B.

SURGERY AND DISEASES OF THE MOUTH AND JAWS. By VILRAY PAPIN BLAIR, A.M., M.D., Professor of Oral Surgery in the Washington University Dental School, and Associate in Surgery in the Washington University Medical School. Pp. 638; 384 illustrations. St. Louis: C. V. Mosby Co.

WITHIN the last year or two an unusual number of new books on this subject have appeared, probably in response to the great demand on the part of medical men for a better knowledge of the mouth and jaws, and on account of a broadening of the field of the dental student. No book hitherto published so well fulfils this dual object as the volume under consideration.

The first chapter is devoted to physical examination and to anatomical considerations, followed by short chapters on general surgical pathology, discussing inflammation, tumors, hemorrhage, shock, wounds, and other injuries, for all of which information the dental student would otherwise have to consult works on general pathology and surgery. Then the various surgical conditions affecting the special parts are taken up in detail, the method of dealing with the different regions separately being followed as much as possible.

For the dental student, the book contains rather more than he requires to know of the major affections of the face and jaws, particularly in regard to treatment. For the general surgeon especially interested in this region of the body, Dr. Blair has provided a reference work of great value.

R. H. I.

HANDBOOK OF THE DISEASES OF THE EAR. By RICHARD LAKE, F.R.C.S., Surgeon to the Royal Ear Hospital, Aural Surgeon to the Seaman's Hospital, Greenwich. Fourth edition; pp. 287; 77 illustrations, including 4 colored plates. New York: William Wood & Co..

THE fourth edition of this manual has thirty-five pages more reading matter and eleven more illustrations than the last edition by the same author in the year 1910.

The book is well adapted for the use of the undergraduate and busy general practitioner, being devoid of unnecessary comments on theories and confusing references to other authors.

B. D. P.

PROBLEMS OF LIFE AND REPRODUCTION. By MARCUS HARTOG, M.A., D.Sc., F.L.S., F.R.H.S., Professor of Zoölogy in the University College, Cork. New York: Science Series, G. P. Putnam's Sons.

THE book is primarily intended for the use of the "cultured laity" but is also of interest to the practitioner who occasionally takes journeys into the field of pure science. The author writes in a popular style, is careful to define practically every term that he uses, and they are many, and lays emphasis upon every topic that may interest the general reader. In spite of this, in some of the chapters, as on cell division he plunges into the subject quite deeply, perhaps a little too much so to hold the attention of those not directly interested in the subject. However, he shows that

he has a good command of the subject and introduces much material which is engaging the attention of researches in this field at the present moment. This is particularly true of the chapter on the "new force" mitokinetism. Far more readable for the general student is the chapter on the transmission of acquired characters. The combative nature of the author is here well seen. After accusing the Weismannists of unfair attacks upon the transmissionists he makes a counter attack. If one seeks a conservative, emotionless, consideration on any subject of which he treats they will seek without success in the pages of this book. The next chapter is a criticism of Dr. G. Archdall Ried's attack as he calls it on modern Lemarekianism. From the standpoint of the general reader the chapter could have been omitted with advantage. The vitalistic view of life is later discussed and the shortcomings of the "mechanical" and "physicochemical" explanations of vital phenomena referred to. Then follows a review of the writings of Samuel Butler. The final chapter is an address to teachers on the teaching of "nature study."

E. L. P.

DISEASES OF THE THROAT, NOSE, AND EAR FOR PRACTITIONERS AND STUDENTS. By W. G. PORTER, M.B., B.Sc., F.R.C.S. Ed., Surgeon to the Eye, Ear, and Throat Infirmary, Edinburgh; Surgeon, Ear and Throat Depart., Royal Hospital for Sick Children, Edinburgh; Aurist to the Edinburgh Royal Institution for the Education of the Deaf and Dumb. Pp. 275; 77 illustrations, 44 in colors. New York: William Wood & Co.

THE author in writing this book has endeavored to provide, in a small volume, the practitioner and students with sufficient information on diseases of the nose, throat, and ear, so that they may have a basic knowledge of diseases of these organs as they appear in general practice and to be able to treat the simpler ones. The book is divided into four sections, one on disease of the pharynx, one on diseases of the larynx, one on the nose, and one on diseases on the ear. It is well arranged and clear and the different diseases are considered in what might be termed their natural sequence.

On the whole the book is well written and easily readable; it is up to date, and, though individual exceptions can be taken to some of the author's statements, it is a safe and reliable guide for those for whom the book was intended, namely, the general practitioner and student.

In the appendix there is a formula containing many useful prescriptions and the index is sufficiently detailed to make it a useful addition to the book.

G. B. W.

THE COMING OF EVOLUTION. By JOHN W. JUDD, LL.D., F.R.S., formerly Professor of Geology and Dean of the Royal College of Science. THE INDIVIDUAL IN THE ANIMAL KINGDOM. By JULIAN S. HUXLET, B.A., Research Associate of the Rice Institute. HEREDITY IN THE LIGHT OF RECENT RESEARCH. By L. DONCASTER, M.A., Fellow of King's College. THE PSYCHOLOGY OF INSANITY. By BERNARD HART, M.D., Lecturer on Psychiatry, University College Hospital Medical School. BREWING. By A. CHESTON CHAPMAN, President of the Institute of Brewing. Cambridge: University Press. New York: G. P. Putnam's Sons.

THESE small volumes of some 150 pages each, represent the recent additions to the Cambridge Manual of Science and Literature. The several authors are authorities in their respective fields and present their subject matter in an entertaining and lucid manner, so that the text can be followed with ease by those unacquainted with the abstruse problems of the various subjects.

These little books, while not actually pertaining to medical subjects could be read with profit by physicians interested in phases of other sciences which have a close bearing upon and intimate correlation with, the science of medicine. J. H. M., JR.

PUBLIC HEALTH CHEMISTRY AND BACTERIOLOGY. A HANDBOOK FOR DEPARTMENT OF PUBLIC HEALTH STUDENTS. By DAVID McKAIL, M.D., D.P.H., F.R., F.P.S.G., Lecturer on Public Health and Forensic Medicine, St. Mary's College, Glasgow; Examiner in Public Health for the Department of Public Health, Scottish Conjoint Board, etc. Pp. 409. New York: William Wood & Co.

THE author presents in this volume a handbook for teacher and student from material he uses in his public health course. It is almost entirely devoted to technical examinations and makes an excellent complement to a book on theoretical and practical hygiene. The first part of the book is devoted to chemical and physical analysis of water, air, soils, food beverages, and disinfectants. The chapter on foods is especially good. The latter two-thirds are devoted to public health bacteriology. Greatest attention is paid to methods of detection and determination. At the end of the book the author devotes a chapter to special examinations of water, air, soil, sewage, and food, and winds up by giving the regulation for the diploma in public health, and a review of Parke's work on bovine and human tuberculosis. As a handbook for the sanitarian it is useful chiefly in the labora-

tory, but there are a few methods given for rapid testing in the field. It will be probably most useful to those giving courses on the subject. No illustrations are given because the apparatus is seen during instruction, the author says in the preface. H. F.

STUDIES IN CANCER AND ALLIED SUBJECTS. From the Departments of Zoölogy, Surgery, Clinical Pathology and Biological Chemistry, Conducted under the George Crocker Special Research Fund at Columbia University. Volume III, pp. 295. New York: Columbia University Press.

THIS book is a series of reprints of various articles by the numerous workers under the Crocker Fund. The reprints are arranged according to departments and preceded in two instances by interesting scientific reports of the departments by their respective heads. It is extremely convenient to have under one cover the diverse but valuable papers contained in this volume.

H. T. K.

AIDS TO DISEASES OF CHILDREN. By JOHN M. CAW, M.D., R.U.I., L.R.C.P. (Edin.), Senior Physician to the Belfast Hospital for Sick Children, etc. Fourth edition; pp. 423. New York: William Wood & Company.

By using very thin paper and small type, the author has managed to put a surprising amount of material between the covers of an apparently small volume. Etiology, pathology, symptomatology and treatment are very fully covered as well as the anatomy and physiology of infancy and childhood.

S. J. R.

ACUTE ABDOMINAL DISEASES, INCLUDING ABDOMINAL INJURIES AND THE COMPLICATIONS OF EXTERNAL HERNIA. By JOSEPH E. ADAMS, M.B., M.S. (Lond.) F.R.C.S. (Eng.), Senior Assist. Surgeon, East London Hospital for Children; Hunterian Professor, Royal College of Surgeons of England, etc., and MAURICE A. CASSIDY, M.A., M.D., B.C. (Cantab.), F.R.C.P. (Lond.), Physician with charge of Out-Patients, St. Thomas' Hospital. Pp. 571. New York: William Wood & Co.

THIS book is based on the experience of the authors as Resident Assistant Surgeon and Resident Assistant Physician respectively

to St. Thomas' Hospital. Its object is "to discuss, compare, and contrast all the various acute diseases and injuries to which the abdomen and its contents are liable, treating these conditions from the point of view of both physician and surgeon." The field is comparatively untilled, the authors' experience is large, and while we may not always agree with their interpretation of "acute," and their method of discussion involves a certain amount of repetition, the result is a most interesting and in many respects, satisfying production. To the hospital surgeon as well as to the general practitioner, it affords much information and food for thought.

E. B. H.

STUDIES IN CANCER AND ALLIED SUBJECTS. THE STUDY OF EXPERIMENTAL CANCER; A REVIEW. By WILLIAM H. WOGLOM, M.D., Assistant Professor, Columbia University, Assigned to Cancer Research. Conducted under the George Crocker Special Research Fund at Columbia University. Volume I; pp. 274; 55 illustrations and numerous charts. New York: Columbia University Press.

THE book is an octavo volume which could easily be bound in smaller compass, a volume occupying more library room than its contents require. As is indicated in the title, the work is a review and places before the reader in condensed form the material on experimental cancer which had been contributed before its appearance. Written in true scientific spirit, well illustrated, clearly printed and with ample references to the literature of the subject, the book commends itself highly to those who wish a brief but comprehensive review of this prolific and prodigious field. H. T. K.

A HANDBOOK OF SURGERY INTENDED FOR DENTAL AND JUNIOR MEDICAL STUDENTS. By ARTHUR S. UNDERWOOD, M.R.C.S., L.D.S. (Eng.), late Examiner Royal College of Surgeons of England, etc., and BAYFORD UNDERWOOD, M.B., B.S. (Lond.), L.R.C.P., M.R.C.S. (Eng.). Pp. 244; 19 illustrations. New York: William Wood & Co.

THIS little volume gives an outline of the general principles of surgery, with special reference to the parts of importance to the dental student. For his instruction also diseases of the eye, nose, and accessory sinuses, larynx, and skin are briefly described. The book should be useful to students preparing for examinations.

R. H. I.

EXAMINATION OF THE NERVOUS SYSTEM. JULIAN LOUDON, B.A., M.B., Assistant in Clinical Medicine, University of Toronto. Pp. 30. Toronto: G. A. Merrick Printing Company.

It is simply an outline for the student so that a complete examination of the nervous system can be made. It is a question whether this is worth while after all, for if one were to follow out rigidly the scheme in its entirety, it would take about a week to examine a patient.

T. H. W.

THE DOCTOR IN COURT. By EDWIN VALENTINE MITCHELL, LL.B., of the Massachusetts Bar. Pp. 152. New York: Rebman Company.

THIS work is not intended to be a treatise on Medical Jurisprudence but rather attempts to outline the relationship which the law bears to the physician on the witness stand, whether he be testifying in his own behalf or as an expert. It presents in a clear and convincing way a knowledge of the physician's duties and legal obligations which may grow out of his relations with his patients.

S. J. R.

THE TREATMENT OF INFANTILE PARALYSIS. By OSCAR VALPIUS, M.D., Professor Extraordinary at the University of Heidelberg. Translated by ALAN H. TODD, M.B., B.S., B.Sc. (Lond.), House Surgeon, Guy's Hospital. With introduction by J. JACKSON CLARKE, M.D. (Lond.), F.R.C.S. New York: William Wood & Co.

VALPIUS has collected in his single volume, valuable facts which are essential in the treatment of infantile paralysis. These facts are drawn from his and many other orthopedic surgeons' experiences in the treatment of the sequelæ of this type of paralysis. He presents this subject in an attractive manner weaving into the subject his personality and his own experiences in such a manner as to impress one of his profound sincerity. It is rarely possible to translate a theme from one language to another without losing something of the author's force or shades of meaning. In the statement of facts, however, it can be done more concisely. This book in point of view of order is unchanged and probably has lost nothing of the original continuity of thought.

This work has, however, the following excellent features: The facts are grouped under headings, which arrangement facilitates reference. The treatment of the various stages and sequelæ

of the disease is carefully outlined and clearly defined. The subject matter is emphasized by explanatory cuts many of which are original. The surgical and mechanical principles employed and the results obtained thereby, seem to be given impartially.

This work should serve to deepen interest in this subject and reflects great credit upon its author. W. J. M.

DISEASES OF THE SKIN. By DAVID WALSH, M.D., Senior Physician, Western Skin Hospital, London, etc. Pp. 298; 29 illustrations. New York: William Wood & Co.

THE writer has prepared a concise and readable little volume, containing a few excellent illustrations. The subject has been divided into disorders of circulation, disorders of nerve origin, common inflammatory dermatoses, disorders of the sebaceous glands, of the sudoriferous glands, of the hair and nails, of pigmentation, of vascular origin, hypertrophic and atrophic dermatoses, newgrowths, parasitic dermatoses, and certain general diseases affecting the skin. The author has made an innovation in classing epidermolysis bullosa and prurigo as angioneuroses under the heading of disorders of circulation. It is also rather debatable whether pellagra should be placed under the parasitic dermatoses, notwithstanding the important investigation of Sambon. The various diagnostic tests, biological investigations, and the newer methods of treating syphilis are described. F. C. K.

THE MICROTOMIST'S VADE MECUM. A HANDBOOK OF THE METHODS OF MICROSCOPIC ANATOMY. BY ARTHUR BOLLES LEE. Seventh edition; pp. 526. Philadelphia: P. Blakiston's Son & Co.

THE usefulness of a book on methods depends very largely on the extent of the personal experience of the author with the manipulations described. By this test Lee's book must be regarded highly, for there is no other author writing in English, who has had such a long and varied experience as the writer of this book on microscopic methods. The book first appeared in 1885, and in the succeeding editions which have appeared in the interval, the revisions have been so complete that each new edition has come to be regarded as almost a necessity for those interested in the preparation of tissues for microscopic study. In the seventh edition the size of the book remains unaltered, but by the omission of out-of-date matter the author has managed to introduce much

new information, more than 700 additional entries appearing in the index. The sections relating to the blood and blood-parasite have been rewritten, and the various modifications of the silver staining of neurofibrils by the methods of Ramón y Cajal and Bielschowsky are described at length. An interesting new item concerns Gilson's Sandarac mounting media, which dispense with the use of clearing agents and confer on unstained or feebly stained objects a greater degree of visibility. This would be especially useful in delicate cytological work. In addition there is the usual good discussion of well-tried methods which makes the book a guide to be trusted, and useful not only to the laboratory worker, but to all seeking information on microscopic technique.

W. F. A.

CLINICAL-SURGICAL DIAGNOSIS. By F. DE QUERVAIN, Professor of Surgery and Director of Surgical Clinic at the University of Basle. Translated from the fourth edition; pp. 779; 510 illustrations and 4 plates. New York: Wm. Wood & Company.

THE author has produced a work that is exceedingly valuable to the student and practitioner. From his position as a teacher he is well fitted to present his subject in a rational, practical, and detailed manner.

The question of diagnosis only is considered. The methods of investigation are those that can readily be used by the practitioner, comprising, the bacteriological, histological, and radiographic phases of the study. The diagnosis in each case is arrived at by a clear representation of important symptoms, they being no useless, theorizing or deviation into purely academic questions.

The work is purely a clinical diagnosis and the reader hunting for help is not burdened by having to read through pages of allied subjects. The book is a good one and well worth careful study.

E. L. E.

HANDBOOK OF DISEASES OF THE RECTUM. By LOUIS J. HIRSCHMAN, M.D., President of the American Proctologic Society, Lecturer on Rectal Surgery and Clinical Professor of Proctology, Detroit College of Medicine. Second edition; pp. 339; 172 illustrations, including 4 colored plates. St. Louis: C. V. Mosby Co.

IN spite of the warning sounded in the chapter on the Limitations of Office Treatment, we feel that the author has fallen into the error, so common among those who write books on special subjects for the use of the general practitioner, of including too

many and too extensive procedures among those recommended as suitable for performance in the office, and that he has so far over-rated the skill of the average practitioner that he has risked placing his readers in the unenviable position of attempting operations they would be unable to carry to successful terminations. This is especially true in regard to the treatment recommended for internal hemorrhoids.

Throughout the book the author insists upon the necessity of making a thorough proctologic examination of the patient, and it is to this frequently repeated advice that much of the value of the book is due.

The book is well printed, and the illustrations are excellent. With the warning given above it may be recommended to the general practitioner as a guide in the treatment of rectal diseases.

S. W. M.

THE FITNESS OF THE ENVIRONMENT. By LAWRENCE J. HENDERSON, Assistant Professor of Biological Chemistry in Harvard University. Pp. 317. New York: The Macmillan Co.

As the title indicates, the author's object is to describe some of the natural phenomena, which are of importance to the life of organisms upon the earth. Those phenomena which he selects for special description are not the grosser aspects of Nature, however, but chemico-physical processes, and concern principally the properties of carbon, hydrogen and oxygen, and their compounds, especially water and carbonic acid. One hears much of the fitness of the organism to the environment, and of the adaptations of different parts of the organism to carry out certain functions. Here is presented the other side of the relationship: the characteristics of some of the elements and compounds which are of fundamental importance in making the environment suitable for the physiological processes of living plants and animals. The conclusion is that Darwinian fitness is a perfectly reciprocal relationship: a fit organism inhabits a fit environment. W. H. F. A.

SYSTEMATIC CASE-TAKING. By HENRY LAWRENCE MCKISACK, Physician to the Royal Victoria Hospital, Belfast. Pp. 166; 1 illustration, New York: Paul B. Hoeber.

THE term "case-taking" must not be confused with history-taking, for the author uses it to embrace the acquiring of all information, both subjective and objective, necessary to make a

diagnosis. The amount of space devoted to the sub-head, pain and to the chapter on the nervous system, seems unnecessarily full, but possibly these subjects have received too scanty consideration heretofore. The work serves to emphasize the too oft neglected fact that only by systematic case-taking can a trustworthy diagnosis be reached.

S. J. R.

LECTURES ON DISEASES OF CHILDREN. By ROBERT HUTCHINSON, M.D., F.R.C.P., Physician to the London Hospital and Physician to Hospital for Sick Children, Great Ormond Street. Third edition. Pp. 404; 69 illustrations and 13 diagrams. New York and London: Longmans, Green & Co., and Edward Arnold.

THE book embodies a series of lectures first given in the London Hospital in 1902, with subsequent revisions, and covers the most important diseases found in infants and children exclusive of the exanthemas and the acute contagious diseases such as diphtheria, pertussis, etc. It is essentially a clinical presentation clearly based upon careful, painstaking and extensive observation, and contains many valuable suggestions, and descriptions not found in the average text-book. Because, however, of the limitation of the number of subjects considered, it cannot be considered in any sense as a text-book upon pediatrics. As very delightful and instructive collateral reading, however, it well deserves a place upon the pediatric book-shelf.

J. C. G.

THE HEALTHY BABY. By ROGER H. DENNETT, M.D., Instructor in Diseases of Children in the New York Post-Graduate Medical School, etc. Pp. 235. New York: The Macmillan Company.

THE book is intended to make clear to the mother the best way to do the every-day things that have to be done for a child, and the author should take satisfaction in having performed his task well. The book is divided into six parts, dealing with development and the bodily functions, hygiene and training, common ailments, care of the special organs, feeding and diet, lists and tables. No attempt is made anywhere to usurp the office of the family doctor or to become the "universal pediatricist." It is a collection of good advice in plain non-technical language, and aims at prevention rather than cure. Feeding and diet is such a large and unsettled subject that it does not pay to be too didactic. This is the only part of the book to which exception might be taken. While a large number of pediatricists will agree

with the sentiments here expressed, there is likely to be a considerable group who would differ with these ideas. The manner of modifying the milk would probably be the chief bone of contention, but there are several minor points which would give ground for difference of opinion. In spite of these objections the work is of value, and the physician who recommends it to his patients will probably earn their gratitude. S. J. R.

SCHOOL HYGIENE. By FLETCHER B. CRESSLER, PH.D., Specialist in School Hygiene and School Sanitation, U. S. Bureau of Education. Pp. 369; 51 illustrations. New York: The Macmillan Company.

In outlining the purpose of his book the author states that it is not written for the specialist in school hygiene but for the busy teacher. Indeed, the final goal of the author's effort seems to be the hardened and custom ridden mind of school boards, reached through intelligent insistence on the part of well informed teachers.

The selection of topics is based on their practical importance and all are treated in a most painstaking way. A. A. H.

TREATMENT OF INTERNAL DISEASES. By PROF. NORBERT ORTNER, of the University of Vienna. Edited by NATHANIEL BOWDITCH POTTER, M.D., Assistant Professor of Clinical Medicine at Columbia University, New York. Translated by FREDERIC H. BARTLETT, M.D., Instructor of Children's Diseases at Columbia University. From the fifth German edition; pp. 640. Philadelphia: J. B. Lippincott Company.

THE second American edition of this therapeutics is translated from the fifth German edition. It follows closely the plan of the previous edition and on the whole has undergone but few changes. Professor Fronz, of Vienna, has entirely rewritten the section on children's diseases, while here and there throughout the text occasional minor changes and additions have been made. The editor has wisely omitted such drugs as are not sanctioned by the Council of Pharmacy and Chemistry of the American Medical Association, but he has retained many which are inactive and totally unknown. A change that would have greatly improved the book would have been to abbreviate the number of prescriptions and at the same time reduce the number of drugs that are found in so many of the formulæ.

Another criticism that might be made is that nothing is said of some of the newer methods of treatment that have come into use since the last edition. For example, nothing is said of the treatment of leukemia with benzol, of the removal of the spleen for pernicious anemia, of vaccine therapy, or fresh air in the treatment of croupous pneumonia, and of many other advances in modern therapy. Even if the author or the editor does not approve of nor advocate such methods, yet would it not be of advantage to the reader to know his experience with these procedures and to know why he does not approve of them? Disregarding these comparatively few criticisms and omissions the book is a splendid compilation of practical treatment—of treatment in all its forms, whether dietetic, hygienic, physical, mechanical, climatic, or medicinal.

J. H. M., Jr.

THE NEW PUBLIC HEALTH. By H. W. HILL, M.B., M.D., D.P.H.,
Director Institute of Public Health, London, Ontario. Pp. 128.
Minneapolis: Press of the *Journal-Lancet*.

IN this book are collected a series of monthly articles on Public Health Topics, which originally appeared in the *Journal-Lancet*, of Minneapolis. It is meant for general reading and especially recommends itself for this purpose by its conciseness, clearness, and the logical way in which the essential factors which comprise the great public health problem are treated.

The author feels that the public or primary routes of spread of disease are thoroughly understood. He therefore lays special stress on the secondary or contact sources of spread. It is in this latter direction that he declares future progress will be made.

The crux of the situation to him is the individual, the fountain head of contagion. He holds universal enlightenment above coercion and outlines a means for its accomplishment.

A. A. H.

DISEASE AND ITS CAUSES. By W. T. COUNCILMAN, A.M., M.D., LL.D., Professor of Pathology in Harvard University. Pp. 254; 19 illustrations. New York: Henry Holt & Co., 1914.

THIS latest addition to the HOME UNIVERSITY LIBRARY is a valuable one, and is of special interest to the medical profession, not in that it contains any new or special information, but in that it puts in the hands of the layman the kind of knowledge he should have for the proper forming of his conceptions of disease as it occurs in his daily experience.

Such simple and clear presentation of basic medical truths is bound to bear its fruit in hastening the advent of a state of general enlightenment.

The author's discussion of disease in its general aspects is good. His more more specific teachings as regards the bacteria, infections, carriers, immunity, chronic disorders, heredity, and eugenics are to the point.

The aim of the book is clear, and is well expressed in the author's words, "No measures of preventive medicine are successful which are not supported by a public educated to appreciate their importance."

A. A. H.

A MANUAL OF OPERATIVE SURGERY, WITH SURGICAL ANATOMY AND SURFACE MARKINGS. By DUNCAN C. L. FITZWILLIAMS, Lecturer on Clinical Surgery and Joint Lecturer on Operative Surgery, St. Mary's Hospital Medical School. Pp. 446; 284 illustrations. New York: William Wood & Company, 1914.

THIS is a text-book for the "apprentice" and "journeyman craftsman of our profession," and is not intended for a "master of the art" of surgery. With this main purpose of the author in mind the reader will find it a well-constructed book of a useful kind. It will be most useful to the undergraduate student, but the surgeon, particularly the younger surgeon, will find it serviceable. It has the compactness to be expected from the author's long service in preparing for examinations. There are few references, quotations, or repetitions, but there is the marked preference for English operations that one would look for from an English author. There is no reference to the Larrey amputation of the shoulder, a brief reference to Wyeth's pins, but no mention of the method of amputation of the hip necessary to make them serviceable. The references to surgical anatomy are appropriate, the discussion of strangulated hernia particularly good, of necessity, less formal than of most operations, but very practical. There is need of a similar discussion of the conservative surgery of the hand and the relative value of the various amputations of the foot. On the whole the book fulfils well the purpose for which it was intended.

T. T. T.

MATERNITY PRIMER. By A. H. F. BARBOUR, M.D., LL.D., Physician to the Edinburgh Maternity Hospital. Pp. 165; 67 illustrations. New York: William Wood & Co.

THIS book is a set of notes for the use of nurses commencing their maternity training. Pregnancy, labor, and the puerperium

are pictured as a normal sequence. Placenta prævia receives especial attention, and the responsibility as well as the limitations of the nurse in such cases are emphasized. The proper treatments in this and other emergencies are clearly given. Sepsis is also closely studied, and is presented as a preventable condition.

A. A. H.

ARTIFICIAL PARTHENOGENESIS AND FERTILIZATION. By JACQUES LOEB, of the Rockefeller Institute for Medical Research. Translated from the German by W. O. R. KING and supplemented and revised by the author. Pp. 322; 87 illustrations. Chicago: University of Chicago Press.

IN this work of Dr. Loeb's is found a *resumé* of his well-known results upon artificial parthenogenesis together with some new material not hitherto published. Through chemical and physical agencies he endeavors to produce the effects of the sperm upon the egg and by this means to arrive at an understanding of that phase of fertilization concerned in inaugurating development. He comes to the conclusion that the formation of a membrane by the egg is the primary cause of its development, and that there is then necessary some agent to stop this process from continuing too far. Membrane formation may be accomplished by the action of any cytolyzing agent. The cytolysis must be stopped when only the surface of the egg is involved, and this is accomplished through the action of hypertonic sea water. Accelerated oxydation follows the superficial cytolysis and this results in cell division. As an explanation of such action Loeb offers the suggestion that the surface of the egg is an emulsion, and that cytolytic agents destroy its stability. Eggs vary in the degree of this stability and some easily exhibit artificial parthenogenesis. Regarding normal fertilization the conclusion is that the sperm, aside from its action in heredity, has the double function of bringing into the egg a cytolyzing agent to start membrane formation and a second to stop the action of the first when this has been accomplished. There are 32 chapters in the book and a general analysis of artificial parthenogenesis and related subjects in various animals is given.

Mc. C.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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The Successful Cultivation of *Leishmania Donovan* from the Blood.
—M. MAYER and H. WERNER (*Deutsch. med. Woch.*, 1914, xl, 67) have had under observation a patient suffering with tropical splenomegaly (kala-azar). Diagnosis was made by the finding of *Leishmania donovani* in the material obtained by splenic puncture; the organisms were cultivated from this material on Nicolle's modification of the Novy-MacNeal medium. The discovery of the parasites in the peripheral blood is usually possible only in the late stages of the disease; in the early stages it is only after prolonged search, and then only exceptionally, that the organisms are found. The authors inoculated a dozen tubes of media with the patient's blood, adding three to five drops to each tube. The tubes were examined every eight days, and after one month five tubes showed a growth of *Leishmania donovani*. The demonstration of viable parasites in the peripheral circulation is of considerable importance because of the possibility of the transfer of infection by blood-sucking insects. Novy has succeeded in cultivating the organisms from the blood of experimentally infected dogs, but the authors have been unable to find a report of a successful culture from human cases.

Hypercholesterinemia and its Role in the Production of Gall-stones.
—According to CHAUFFARD and his pupil, Grigaut (*Presse. Méd.*, xxi, 929 to 932), whose method was used in the cholesterin determinations, there occurs a true hypercholesterinemia in cases of jaundice, gall-stones, typhoid fever, and pregnancy. In typhoid fever this develops after the febrile period and becomes maximum at about

the seventh month of pregnancy. The cause in these conditions is to be found in a hyperactivity of the adrenals, and perhaps in the corpus luteum as well. It is clearly recognized that typhoid and pregnancy are potent predisposing causes of gall-stones, an essential condition for the formation of which is an excessive blood content in cholesterin. The author calls attention to the exogenous or dietetic origin of cholesterin, since this has some therapeutic importance, and the endogenous, arising mainly from the adrenal glands. A normal function of the liver is to rid the blood of a certain amount of cholesterin, this being excreted in the bile through the specific activity of highly specialized hepatic cells, which may further convert some of it into solvents for cholesterin itself, namely the biliary acids. When these cells fail in their normal functioning, as in cholelithiasis, one finds the adrenals unusually deficient in cholesterin, while the blood contains an increased amount and the bile is deficient in its acid content. Since all these things are evidences of one and the same thing—hepatic insufficiency—one may attribute the formation of gall-stones to a specific disturbance of certain liver cells.

Experimental Production of Pernicious Anemia.—ADLER (*Jour. of Med. Research*, xxviii, 199 to 226), having determined that the severe anemia caused by infections with *Dibothriocephalus latus* is due to the presence of an insoluble fatty acid capable of producing hemolysis, has been able to produce the blood picture of pernicious anemia by feeding dogs large doses of insoluble fatty acids, such as olive oil. The organism normally possesses a defensive mechanism against such acids in the shape of lymph glands, according to the author. As the result of experiments the author concludes that fatty acids are toxic directly in proportion to their insolubility. Animals given non-toxic doses over a long period of time showed some typical blood crises such as are seen in pernicious anemia. The simultaneous administration of suitable amounts of quinine protects the animals from the poisonous effects of the fats. The anemia induced is essentially due to the destructive action upon the circulating red-blood cells, for in the early stages at least the bone-marrow appears to be stimulated so that high red counts may occur. The opinion is advanced that the hemolytic substance occurs in the form of colloidal particles the effects of which depend probably upon the relation of their number to that of the red-blood corpuscles.

A Contribution to the Study of Cancer.—E. WEISS (*Deutsch. med. Woch.*, 1914, xl, 66), alludes to the possibilities of the Abderhalden test as applied to the diagnosis of cancer. The author has made interesting observations which bear on the diagnosis of gastric cancer. He finds that normal individuals, after the parenteral administration of anatomically normal gastric mucosa, develops ferments in the blood serum specific for this tissue. Repeating the experiments with the sera from two patients suffering with cancer of the stomach, he found that there was a failure to develop these ferments. If the observations prove correct when repeated with a large number of cases, he believes it may be possible to apply the method as an exact differential diagnostic aid.

Renal Diabetes.—H. SALOMON (*Deutsch. med. Woch.*, 1914, xl, 217) prefers the name diabetes innocens for the symptom-complex usually designated renal diabetes. Numerous cases have come under the author's observation in von Noorden's clinic. He finds that the condition can remain quite stationary for as long as ten years; that it often runs in families; that it is a comparatively common disease; and that a minority of the cases may exhibit an increase in the blood sugar. The clinical picture of the disease, as the author has observed it, is briefly as follows: There is a harmless glycosuria, often appearing on brothers and sisters. The onset is usually in childhood, even in infancy. A well-marked nervous temperament may be noted in those affected with the disease. The sugar in the urine is usually below 1 per cent., though occasionally for a day or in a single specimen the percentage may be considerably higher. Often mental excitement may cause an increase. The condition suggests the inability of the kidney to secrete a concentrated urine, as in diabetes insipidus. As a rule the low percentage of sugar distinguishes the condition from juvenile diabetes mellitus. Generally the total excretion of sugar with the patient on a mixed diet does not exceed 12 gm. daily. The sugar excretion is only slightly affected by putting the patient on a starch-free diet. Administration of 100 gm. glucose on a fasting stomach is followed by the excretion of not more than 10 per cent. of this amount, usually only 1 to 7 per cent. At the same time the blood sugar rises by 1 to 3 cg. (0.01 to 0.03 per cent.), though a greater increase does not invalidate the diagnosis. Ordinarily the blood sugar is present in normal amount with renal diabetes, though there may be a hyperglycemia. There is no tendency of the disease to progress. In some patients there may be a marked acetonuria on a starch-free diet; this rapidly vanishes when starch is added. Except for the nervous manifestations the patients appear to be normal individuals, and are not more subject than the normal to the usual complications of diabetes mellitus (furunculosis, neuritis, etc.). This seems to hold good also for diabetes innocens with hyperglycemia. Salomon recommends a diet for these patients containing carbohydrate equivalent to 100 to 200 gm. white bread, but after the condition has persisted unchanged for several years a more liberal diet may be allowed.

Further Observations on the Chemotherapy of Experimental Trypanosome Infections.—W. KOLLE, O. HARTOCH, and W. SCHURMANN (*Deutsch. med. Woch.*, 1914, xl, 212) have continued their observations on the treatment of experimental trypanosome infections with antimony preparations. As in their earlier work, they have continued to obtain very good results with antimony trioxide, which they designate "trixidin." Their studies show that: (1) *Therapia sterilisans* by means of trixidin can be accomplished in the case of chronic trypanosome infections of large animals. (2) In cases in which abscess formation has followed the intramuscular injection of trixidin, they have resorted to intravenous administration of antimony trioxide in physiological salt solution with success (rabbits, guinea-pigs). (3) A permanent sterilization of dogs suffering with chronic dourine infection may be accomplished by means of inunctions with antimony preparations. The most potent of these is apparently dimethylphenylpyrazolon-

antimony trichloride in the form of a salve. (4) The principles of treatment developed by the authors, *i. e.*, inunction, or intramuscular injection of water-insoluble (depot-forming) antimony preparations, are applicable to human cases, though it must be remembered that subcutaneous or intramuscular administration is likely to lead to abscess formation. (5) Antimony trioxide may be employed in colloidal-like solution intravenously, at least in small animals. In this form it is very active therapeutically. (6) The authors hope to determine whether the colloidal-like solution of antimony trioxide can be used in the treatment of sleeping sickness of man, possibly as an adjuvant to inunctions.

Loss of the Hypophysis, with Fatal Issue.—M. SIMMONDS (*Deutsch. med. Woch.*, 1914, xl, 322) reports a case with autopsy findings. The patient was a woman, aged forty-six years, who became ill with severe puerperal sepsis. There was a septic necrosis of the hypophysis, the author believes. As a result of the injury to this important organ the following symptoms made their appearance: menopause, muscular weakness, vertigo, attacks of loss of consciousness, anemia, rapid aging; in short, "senium precox." The part of the gland which remained intact doubtless gradually atrophied in the connective tissue surrounding it. The organ became absolutely insufficient and the patient died in coma. At autopsy the only adequate cause of death to be found was an almost total loss of the hypophysis.

The Blood in Hemophilia.—HOWELL (*Arch. Int. Med.*, 1914, xiii, p. 76 to 95). After describing in considerable detail the methods used in the preparation and estimation of antithrombin and prothrombin, Howell gives his observations made upon undoubted cases of hemophilia, studied over a period of two years. The coagulation time was determined by aspirating 2 or 4 c.c. of blood from a vein, and expelling it at once into carefully cleaned test-tubes: by this method the normal coagulation time varies between twenty and forty minutes, the end point being that time at which it was possible to invert the tube. Hemophilic blood coagulates in from two and one-half to five hours, provided the needle of the syringe enters the lumen of the vein on the first puncture. This great retardation of the normal process Howell believes is due to a true reduction in the amount of prothrombin, as a result of which the antithrombin content is relatively greater in hemophilic blood than in the normal specimen with which it is controlled. This peculiarity of the blood can be readily tested for clinically by first oxalating the blood, which is then centrifugalized to secure a clear plasma. If on adding to this plasma a suitable amount of calcium chloride, coagulation is delayed beyond nine to twelve minutes, one may reasonably suspect the existence of a hemophilic condition of that particular blood. Howell presents clearly his arguments against the numerous theories advanced by Morawitz, Wright, Wolf-Sahle, and others, which attempt to attribute the delayed coagulation time to deficiencies in thrombokinase, calcium, thrombozym, etc., and concludes by defining hemophilia as "a condition limited to the male in which the coagulation time is markedly prolonged in consequence of a deficiency in the amount of contained prothrombin, with the additional

characteristic that the defect is transmissible by heredity in accordance with the so-called law of Nasse." Though the ultimate cause is not certain the most likely one is that there exists some functional change in the blood platelets, since these appear to be the source of prothrombin. In studies upon thrombosis, Howell finds here the evidences of diminution in the antithrombin content of the plasma, prothrombin being normal, while in the so-called hemorrhagic conditions both of these constituents show no variations from the normal.

The Surgical Treatment (Splenectomy) of Diseases of the Blood.—R. MÜLLER (Deutsche med. Woch., 1914, xl, 377) has had considerable experience with splenectomy in diseases of the blood. He reviews his own cases, together with those reported in the literature. He finds that: (1) Splenectomy is indicated in infectious diseases, such as typhoid and sepsis, only in case of spontaneous rupture of the spleen. (2) In malaria splenectomy has no effect on the disease. It is indicated here only where there is danger of twisting, in the case of wandering spleen, or in the rare instances where rupture occurs. (3) In leukemia extirpation of the spleen is contra-indicated. (4) In Banti's disease splenectomy if performed at the right time may result in a cure. Even in the third stage, splenectomy combined with a Talma operation may bring about a cure. (5) Severe cases of anemia splenica infantum may be saved by splenectomy. (6) In hemolytic icterus extirpation of the spleen seems to have had a very beneficial effect in a number of cases. (7) A considerable number of cases of pernicious anemia have been improved by splenectomy. In other instances the operation seems to have had no effect. The indications for operation are as yet uncertain. Caution should be exercised if there is any tendency to bleed.

The Diagnosis of Uremia by Means of Indican Determinations in the Blood-serum, Exudates, and Transudates.—G. DORNER (Deutsche. Archiv f. klin. Med., 1914, cxiii, 342) has studied the indican of the blood and other body fluids in nephritics with uremic symptoms and in other patients with convulsions, following the suggestion of Obermeyer and Popper, who believed they had established the fact that a marked increase of the pigment in the blood is practically diagnostic of uremia. The technique was as follows: 10 to 20 c.c. of blood obtained by venesection or syringe were precipitated with five times the volume of 95 per cent. alcohol and filtered. The filtrate was evaporated and the residue taken up in water. This was precipitated by the addition of two to three drops of lead acetate solution, filtered and made up to 10 c.c. by the addition of water. A like amount of Obermeyer's solution was then added. The mixture was shaken in a water-bath with 1 c.c. of chloroform. A more or less intense blue color in the chloroform indicates a positive test. Dorner studied 26 patients; 7 of these had well-marked uremic symptoms and 2 suspected uremia. His conclusions were: (1) The presence of indican in the blood in large quantity is characteristic of outspoken uremia. (2) When indican is present in the blood in considerable amount it is also found in pleural exudate and anasarca fluid, but not in the spinal fluid. (3) No toxic effect can be attributed to the indican in uremia. (4) In uremia due

to lack of kidney tissue (cystic kidney autopsy) indicanemia may be absent. (5) With marked indicanuria without disease of the kidneys, indican is not found in the blood-serum in large amount. (6) It is not certain that the urinary indican is formed in the liver. It is quite possible, Dorner believes, that the kidneys are concerned in its formation. (7) The appearance of indican in the blood or transudates is a sign of approaching exitus, as a rule. However, patients with a small amount of indican in the body fluids may improve.

On the Use of Salvarsan-copper.—G. BAERMANN (*Münch. med. Woch.*, 1914, lxi, 1) reports his results in treating 45 patients suffering with amebic dysentery, frambesia, and malaria with Ehrlich's new compound, which for brevity's sake is called K₃. The number of cases treated is small and permits of no definite conclusions, but the results seem to show that the compound is a very active one. The drug may be given in 0.1 gm. dose on each of three successive days, or 0.15 gm. on two days. The latter is the maximal dose. Baermann found that the drug was entirely useless in the treatment of amebic dysentery. In frambesia it is markedly spirocheticidal. Baermann's impression is that it is more active in this disease than salvarsan. In 1 case of quartan malaria with schizonts and free gametes the parasites disappeared from the blood. In 4 cases of tertian fever with schizonts and gametes no parasites had been found two months after treatment. In 2 cases of pernicious malaria, with rings but no gametes, cure resulted (no parasites after two months). In cases of pernicious malaria with crescents the latter were unaffected, though the schizonts were destroyed. In 1 case of leprosy there was apparent improvement following the treatment. Baermann plans to continue his study and considers the results with frambesia and malaria very encouraging.

A Standard Antigen for the Wassermann Reaction.—C. W. FIELD (*Arch. Int. Med.*, 1914, xiii, 790). The antigen herewith described has been subjected to exhaustive study at the Bellevue Hospital during the past six months, and has been tried over a series of 5000 cases. The antigen consists of an alcoholic extract of guinea-pigs' hearts, half saturated with cholesterin. It is prepared as follows: 300 grams of guinea-pigs' hearts are extracted with 3 liters of absolute alcohol at 37° C. for two weeks. To one-half of the filtrate cholesterin is then added in excess and after having stayed in the incubator over night the solution is exposed to a constant temperature of 16° C. for three hours in order to throw down the excess of cholesterin. The solution is now filtered and is then added to an equal volume of the original alcoholic extract; 20 c.c. of this mixture are then evaporated to dryness at 56° C., desiccated over sulphuric acid for twenty-four hours, and then weighed. In this way is determined just what the total lipid-cholesterin concentration of this alcoholic solution is. For diluting, enough of the alcoholic extract is added to normal salt solution sufficient to make the concentration of the lipoids and cholesterin equal to 0.1 mg. per cubic centimeter; five different antigens made in this manner have been remarkably constant in their total lipid concentration as well as in their anticomplementary and antigenic values.

SURGERY

UNDER THE CHARGE OF

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The Diagnosis of Acquired Diverticulum of the Large Intestine and Sigmoid Diverticulitis.—DE QERVAIN (*Deut. Ztschr. f. Chir.*, 1912, cxxviii, 67) made a study of this subject based upon three cases of sigmoid diverticulitis. In the first, an acute case, the diagnosis was made at operation. In the second, a chronic case, the diagnosis was made before operation. The third case, acute, was seen by an assistant in his absence. When in an old patient acute or chronic disturbances develop in the region of the sigmoid flexure the possibility of diverticulitis should be considered, more particularly when the signs of of acute peritoneal irritation and pain in the left side of the pelvis are present. The diagnosis is made certain with the aid of the rectoscope if one succeeds in passing it high enough. Since the employment of force is forbidden the examination is often unsuccessful. Moreover, peritonitis or a suspicion of abscess will exclude this method of examination. In diverticulitis the x-rays can show only the signs of a diverticulitis by the faulty filling of the sigmoid flexure. The proof of the filling of the diverticulum, after partial evacuation of the bismuth injection, is of value in the diagnosis by the x-ray. This method of examination of the remains of the bismuth injection permits one to recognize, generally, pathological conditions of the large intestine which can not be recognized either by the administration of the bismuth by mouth nor by the ordinary bismuth injection. The functional x-ray examination, that is, the administration of the bismuth by mouth, in diverticulum disease, gives a moderately distinctive picture, only when the feces reach the rectum in a more or less fluid condition. When the feces are firm, the diverticulum does not show clearly, and can give rise to error.

The Influence of the X-rays on the Formation of Callus.—SALVETTI (*Deut. Ztschr. f. Chir.*, 1914, cxxviii, 130) made experimental investigations on rabbits to show the influence of the x-rays on bone healing. He concludes that they produce an irritation on broken bone. At first, this interferes with the formation of callus by the production of a large number of cartilage cells and favors their greater persistence. This interferes with the transformation into the osteoblastic tissue, and is a cause of the weakening of its support. The latter effect of

the irritation of the x -rays upon the healing of fractures—upon the deposition of lime salts in the bone cells—is not so detrimental. This effect is not, in Salvetti's opinion, dependent upon the other two (the greater production of cartilage cells and their lack of firmness), but is due to special factors brought about by the x -ray, which favors the greater accumulation of lime salts. Morpulgo, from his exact and numerous experiments, is positive that the calcifying function of the cartilage cells are in accord with those demonstrated for anabolic and katabolic processes of other substances (fat glycogen). Salvetti believes that if the fracture is exposed to the x -rays in the later stages of consolidation, a more effective deposition of lime salts occurs. In this way we can obtain a sure advantage from this property of the x -ray, in the healing of fractures, especially in fractures with faulty or delayed consolidation.

Iodin Vaporization in the Treatment of Tuberculous Cystitis.—NORMAND (*Jour. d'Urolog.*, 1914, v, 271) introduces into tuberculous bladders, the vapor of nascent iodine by a special apparatus. It was employed in twenty-four cases and is indicated, particularly, in tuberculous cystitis or tuberculous bladders after removal of a tuberculous kidney. It will give equally encouraging results in cases in which bilateral renal and pulmonary lesions or any other tuberculous focus contra-indicate nephrectomy. It should not be employed in acute attacks of reno-vesical tuberculosis or general tuberculosis, for a time at least. Normand has tried to demonstrate the value of iodine vaporization and to give its exact indications. On the other hand he has tried to overcome the causes of error in the technique of its application and to avoid the painful reactions which constitute the most serious objection raised against the method. It is not claimed to be a panacea against tuberculous cystitis, but he believes it is the most valuable therapeutic agent we have for this affection. If the cures are not more frequent, if he finds it impossible to certify that the cures are permanent, he can, at least, say that there follows a general improvement and relief, and that the method is not accompanied by any danger if it is administered carefully. When one considers the agony which these poor patients experience, whose existence is rendered almost intolerable by the frequent and painful micturition which interrupts sleep and causes a serious drain on the nervous system, the relief afforded by iodine vaporization becomes very important.

Prostatism.—WADE (*Annals of Surgery*, 1914, lix, 321) presents a very valuable study of this subject. He says that three outstanding diseases lead to prostatism: (1) Prostatic hypertrophy or chronic lobular prostatitis; (2) prostatic fibrosis or chronic interstitial prostatitis; (3) prostatic carcinoma. The first is by far the commonest cause (82 per cent. of specimens examined). Chronic lobular prostatitis is a senile hyperplasia, an aberrant overgrowth of tissue, not an independent new growth but liable to develop into the same. Chronic lobular prostatitis usually produces prostatic hypertrophy. It virtually always develops in the middle lobe and is almost uniformly confined to the middle and lateral lobes. The gland, in consequence, undergoes changes that usually permit its easy removal by suprapubic prostatectomy. Chronic

lobular prostatitis may develop in and be confined to the anterior lobe. He observed it in one case. It may cause prostatism without enlargement of the organ, intravesical herniation or complete false capsule formation. In these suprapubic prostatectomy is difficult and dangerous. Its success depends on the presence of advanced hypertrophy due to chronic lobular prostatitis. The recognition of this clinically is frequently very difficult. In the advanced type the urinary tract and general health have usually suffered serious damage from the disease. It is therefore justifiable to delay operation in an early case of chronic lobular prostatitis in order to permit of the gland undergoing those hypertrophic changes that facilitate its easy removal by suprapubic prostatectomy. The mortality attending suprapubic prostatectomy is mainly due to the impaired health of the patient prior to operation. The actual cause of death in such cases is usually a local infection arising out of the wound inflicted. The operation of prostatectomy by blind enucleation is unsuitable in cases of prostatism due to other causes than advanced chronic lobular prostatitis. Perineal prostatectomy is a most suitable operation for such cases. Perineal prostatectomy permits the removal of the disease when its presence is diagnosed in all cases. It is, therefore, at present the operation that offers the best prospect of further advance in the treatment of prostatism. For its successful performance an accurate knowledge of the anatomical structure and relationships of the prostate is necessary as well as an understanding of the pathology of the disease. The suprapubic transvesical route by visual dissection offers the prospect of developing into a method of treating prostatism that may ultimately warrant its adoption in a large number of cases. Chronic interstitial prostatitis is best treated by division and removal of the constriction by the transurethral route. Prostatic carcinoma may be in an early case clinically indistinguishable from hypertrophy due to chronic lobular prostatitis. This fact is therefore a further reason for early operation in all such cases. Prostatic carcinoma when recognized clinically may be successfully treated by excision of the gland in suitable cases.

Operative Intervention in Cystic Disease of the Kidneys.—MICKANIEWSKI (*Jour. d'Urolog.*, 1914, v, 603) says that because cystic degeneration of the kidney is usually bilateral the treatment should be considered as palliative and not curative. It is indicated in intolerable pain, suppuration of the cyst, persistent hematuria, hydronephrosis, displacement of the kidney, and anuria. The function of the supposedly good kidney should be proved to be good by catheterization of the ureters and examination of the urine from each kidney. If the function of one kidney is good, one is justified in doing a nephrectomy. In cases with complications, as suppuration of the cyst, impossibility of fixing a movable kidney, or very abundant and persistent hematuria, no other method of treatment is to be employed. If the kidney supposed to be damaged is considered incapable of performing the whole urinary function, or if the kidneys are simply polycystic, conservative operations are indicated. In case of a suppurating kidney, nephrectomy alone can be employed, but it should be done only if it is absolutely necessary. It should never be done in the presence of anuria. If there is a dis-

placed, large movable kidney, nephropexy should be done and at the same time decapsulation with excision of the cysts. In all other cysts, punctures and incisions of the cysts should be rejected, and the preference given to partial nephrectomy or, better still, decapsulation with excision of all the cysts.

A New Symptom of Fracture of the Patella, with a Contribution to the Treatment.—DREYER (*Zentralbl. f. Chir.*, 1914, xli, 931) calls attention to an interesting observation in a case of fracture of the patella with a considerable separation of the fragments. He applied an extension apparatus with adhesive strips on the Buck principle. The adhesive strips were applied only from the thigh down to the knee, but not over the line of fracture, so that the traction was applied only to the thigh and upper fragment of the patella. He found that with active traction the patient could raise the whole limb, extended at the knee, but this was impossible as soon as the traction was removed. This proved that the lateral expansions of the quadriceps aponeurosis at the knee were not torn, as one would have supposed them to have been torn in an ordinary clinical examination. The fracture was treated conservatively with this traction apparatus in action. After twenty-eight days, with the knee fixed for precaution, the patient could walk about. Eight weeks after admission he could flex the knee to an angle of 40 degrees, could raise the whole limb fully extended at the knee, and could walk up and down steps without support. The Roentgen ray showed that the separation of 1 cm. at the time of fracture had been reduced to 2 mm., and the clinical examination showed firm bony union. Dreyer believes that with the aid of this symptom (described above) we can diagnose the preservation of the lateral expansions of the quadriceps aponeurosis and thus decide between the cases which must be operated on and those which may be treated conservatively.

The Technique of Gastrectomy.—FINSTERER (*Deutsch. Ztschr. f. Chir.*, 1914, cxxviii, 564) says that in all cases of carcinoma and very small tumors near the pylorus all of the lesser curvature of the stomach to the esophagus should be excised in order to remove the whole lymph-node region of the lesser omentum. The anastomosis between the stomach and duodenum should be made by lateral implantation of the first loop of the jejunum as close as possible to the plica duodeno-jejunalis. By suturing the edges of the opening in the mesocolon to the gastric stump the anastomosis itself is made to sink into the free peritoneal cavity. For the closure of the duodenum it is sufficient to ligate the crushed stump and invert it by a purse-string suture. When the carcinoma encroaches upon the right wall of the esophagus the suture of the latter can be secured by surrounding it, as by a wrist-band, with folds of the fundus of the stomach. Whether a carcinoma is operable or not, it can be decided only by an exploratory laparotomy and a persistent effort at mobilizing the tumor, since the latter can become fixed by old inflammatory adhesions. The enlargement of the regional lymph nodes up to the esophagus does not contra-indicate resection, because the nodes on the one hand are not of necessity carcinomatous and on the other hand by this method can be completely removed.

An exact cleaning out of all the regional lymph nodes is to be done. Resection is justifiable as a palliative operation, since the removal of the foul and bleeding tumor can lead to a more easy and rapid improvement of the patient than can a gastro-enterostomy. It will provide an undisturbed gastro-intestinal function, while in advanced cases the gastro-enterostomy opening will soon be involved in the growth.

Arthritis of the Acromioclavicular Joint as an Important Feature in the Pathology of Obscure Shoulder Injuries.—SIEVERS (*Deutsch. Ztschr. f. Chir.*, 1914, cxxix, 583), in the Trendelenburg Festschrift number, calls attention to the importance of the acromioclavicular joint in the movements of the arm and shoulder. It is frequently affected in obscure shoulder injuries, which are due either to falls on the shoulder or to force transmitted from the elbow or hand. These traumata give rise to degenerative inflammatory affections of this joint, which are demonstrable by the Röntgen rays in the form of acute or chronic arthritis of this joint. It may be associated with fracture of the acromial end of the clavicle. The condition may exist alone or be combined with other traumatic affections of the shoulder-girdle or shoulder-joint. The diagnosis rests chiefly upon the disturbance of the functions of the joint, especially of its movements. Often there will be symptoms localized to the joint, consisting in demonstrable changes in the joint and subjective disturbances. The Röntgen rays should be employed in every case and a röntgenogram of each shoulder should be taken for comparison. The condition causes severe pain and disturbance of movements and long-continued inability to work. The acute form should be treated by rest and novocain injections into and around the joint. The chronic form, in many cases, will resist the usual therapeutic measures. After a sufficiently persistent trial of these, without success, resection of the acromioclavicular joint with implantation of a fatty flap between the ends of the bones will give a satisfactory result. The operation should aim at mobilization and not at ankylosis of the joint.

Original Surgical Uses of the Bone Graft.—ALBEE (*Surg., Gynec., and Obst.*, 1914, xviii, 699) says that his experience as to the trustworthiness of the bone graft, as a surgical agent, when taken with its enveloping membranes (periosteum and endosteum) and contacted with bone, has been borne out by Murphy, McWilliams, and others, who have obtained practically 100 per cent. of successes. In his last 100 cases the successes have been 100 per cent. The endosteum, marrow substance, and periosteum should be included in the graft, as they play a most important role in aiding to establish an early and sufficient blood-supply from the recipient tissues to the cortical part of the graft. The endosteum is also actively osteogenetic as well as the inner layer of the true periosteum. A rapid and complete union between graft and recipient bone should in many cases be enhanced by the interposition of numerous small grafts in which the periosteum may be disregarded because of the easy access of blood-supply to their interior osteoblasts. These coalesce with each other and with the recipient bones and the large graft. The living bone graft has certain

bacteria-resisting properties, as evidenced by two of his animal experimental cases where sepsis occurred and parts of each graft became united to the recipient bones, while the rest of the transplant succumbed to the infection and requadrated. The bone graft apparently acts always as a stimulus to osteogenesis to the bone into which it is ingrafted or contacted. The bone graft when well contacted becomes immediately adherent to the recipient bone by newly formed tissue, which changes to solid bone within four weeks' time. This together with its bacteria-resisting property strongly favors, in Albee's opinion, the substitution when feasible of the bone graft in place of all metal internal splints, especially when it is appreciated that metal has the opposite effect to the graft, in that it inhibits callous formation, produces bone absorption, and favors infection. The dowel, the inlay, and wedge bone graft afford a means of repairing and remodelling the skeleton which the surgeon has not hitherto possessed.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Uterine Carcinoma with Cancerous Ascitic Fluid.—GREEN and KOURAD (*Boston Med. and Surg. Jour.*, 1914, clxx, 352), reports 6 cases of inoperable uterine carcinoma treated by subcutaneous injections of cancerous ascitic fluid. The authors were led to try this method of treatment because of the occasional relief from pain and the temporary retardation of growth that had been observed following similar treatment by Hodenpyl and Risley. An abundance of such fluid was obtained from one of the cases, and with this fluid autogenous inoculations were made in her case and heterogenous in five other patients. The treatment was continued in some instances over a period of four months. The reporting of this series of cases has been delayed for two years, in order to determine as far as possible whether the results obtained were permanent. These cases all showed a slight and irregular elevation of temperature, which, however, bore no apparent relation to the injections of cancerous ascitic fluid, but seemed rather to be due to septic absorption from the ulcerating surface of the cancer. The results obtained correspond with those obtained by Risley at the Massachusetts General Hospital. Three cases gave no apparent reaction; two patients, according to their own statement, were relieved of pain and improved in general physical condition; the third showed an apparent temporary relief of pain, and the tumor sloughed, apparently as a result of the treatment, as evidenced by the passage of necrotic tissue per vagina. Four of the patients died of the disease and apparently without retardation. Two others were discharged and lost to observation. The authors believe that these injections have

a beneficial effect, but whether this effect is due simply to a serum isotonic with the blood and acting as a stimulant or whether the action is specific remains still to be proven. Patients with extensive cancer are usually cachectic and ill-nourished, and therefore it is easy to conceive that the injection of a highly nutritive fluid would have a stimulating effect and aid in improving the general condition and thus probably add to the resistance against the cancer. The authors are of the opinion that the action of such serum is slight, temporary, and shows little or no specificity.

The Influence of Calcium Chloride on Diuresis in Chronic Nephritis.

ARNOLDI and BRÜCKNER) *Ztschr. f. klin. Med.*, 1914, lxxix, 300) give their tabulated findings that show that calcium chlorid in small doses is able to cause considerable diuresis in chronic nephritis. This effect was especially observed in cases of nephritis associated with edema and scanty albuminous urine. In order to secure the maximum diuretic action of calcium chloride, they advise that the intake of fluids should be moderate, not over 26 c.c. per kilogram of body weight. The excretion of albumin was not appreciably influenced in 3 cases, in 5 cases the amount of albumin was more or less diminished and in no case was the albumin increased by the treatment.

Artificial Pneumothorax.—SCHAIE (*Jour. Amer. Med. Assoc.*, 1914 lxii, 900) reports 45 cases of pulmonary tuberculosis in which the induction of artificial pneumothorax was attempted for therapeutic purposes. A complete pneumothorax was obtained in 21 cases and a partial pneumothorax in 18 cases, while in 6 cases the attempt resulted in failure; 8 cases have given brilliant results. In cases with high fever the results have been most striking. Previously in all these cases there has been persistent fever for periods varying from three to eight months, and the patients had suffered from great loss of weight, chills, and sweats. In all of this group the temperature has remained low or normal since the induction of the pneumothorax, a length of time now varying from six months to one year. In 3 other instances, active and advancing processes have been arrested; 7 cases of hemorrhage were treated, but in one of these cases the attempt to produce a pneumothorax was unsuccessful; 4 patients have had no recurrence of their hemoptysis during periods varying from six months to a year. In one patient the result was partially successful, as the patient has only occasionally spit blood since the operation. Another case has been treated too recently to know what the results will be. It was noted that in 8 cases there was an increase in the signs in the untreated lung; 5 of these had shown a slight tuberculous involvement in the other lung when treatment was begun; the rest apparently developed entirely new processes

The Technique and Action of Subcutaneous Injection of Neosalvarsan.—WECHSELMANN and EICKE (*Münch. med. Woch.*, 1914, lxi, 535) advise the more frequent use of neosalvarsan by subcutaneous injections. They have given over 7000 such injections without serious accident. They inject from 0.3 to 0.45 gm. neosalvarsan dissolved in 0.5 c.c. of hot 0.7 per cent. salt solution. The most important point

in their technique is to deposit the neosalvarsan solution directly upon the fascia. The details of the technique are given with the precautions necessary to secure this result. When given properly these injections are not painful, and painful infiltrations or abscesses do not result. Toxic symptoms from too rapid absorption of neosalvarsan also do not occur. Wechselmann and Eicke no longer use mercury for the treatment of syphilis, and claim that neosalvarsan is more effectual in controlling the disease.

The Use of Salicylic Enemas in Dysentery.—LUTSCH (*Münch. med. Woch.*, 1914, lxi, 476) has tried Eichhorst's method of treating dysentery by rectal enemas of a 2 per cent. solution of sodium salicylate, with excellent results. He says that pain and tenesmus are both promptly relieved by this method of treatment. The salicylate injections are given at body temperature, and should be retained for half an hour. The dose for an adult is 13 gm. of sodium salicylate in 650 c.c. of water. Lutsch has also used these salicylate injections for the treatment of ordinary diarrheas and catarrhal intestinal conditions, with striking results.

The Danger and the Prevention of Anaphylaxis from Antitoxin.—JOSEPH (*Deutsch. med. Woch.*, 1914, xl, 545) believes that the danger of anaphylaxis in man has been much exaggerated. He does not believe that the phenomenon of anaphylaxis which is observed so frequently in small animals occurs so often in man. The danger of anaphylaxis exists principally in much debilitated children, and when the antitoxin is given intravenously the second time. Joseph thinks that any danger of anaphylaxis could be avoided by using antitoxin obtained from cattle instead of from horses. This could be used for prophylaxis, reserving antitoxin derived from the horse for use in cases of actual diphtheria. Anaphylaxis can also be avoided by inducing anti-anaphylaxis by a preliminary subcutaneous injection of a minimal dose of the antitoxin. This prepares the body in such a way that the injection of a curative dose of antitoxin a few hours later has no power to induce anaphylactic reaction. Friedberger and Mita avoid anaphylaxis by slow intravenous injections of antitoxin, a drop at a time. Joseph claims that any of these methods renders the recipient refractory to any anaphylactic reaction without regard to the method of the administration of the antitoxin.

Salvarsanized Serum in Syphilitic Diseases of the Central Nervous System.—AYER (*Boston Med. and Surg. Jour.*, 1914, clxx, 452) concludes from the use of salvarsanized serum in tabes, paresis, and cerebrospinal syphilis that the method as given by Swift and Ellis is entirely without danger. This method of treatment is effective in many cases where other treatment has failed. It undoubtedly attacks syphilis from the etiological point of view, thus tending to cure the disease as well as relieve the symptoms. The most satisfactory effect of the treatment is seen in the group of cerebrospinal syphilis, in which a complete cure may be obtained in some cases. In tabes arrest of the disease is often possible by this method of treatment, but in general paresis this treatment is least effectual, although in the preparetic

stage encouraging results may be obtained. Ayer is of the opinion that persistent treatment by this method is the most important point in the successful use of salvarsanized serum. Owing to the complicated technique of administration and the necessity to control this treatment by careful examinations of the spinal fluid as to protein content, cell count, Wassermann, etc., Ayer does not expect to see this treatment in general use. He believes it should be employed when other methods of treatment fail in whole or in part, or when haste is required in order to save vital tissue.

Active Immunization against Diphtheria.—SCHREIBER (*Therapie de Gegenwart*, 1914, lv, 97) has applied Behring's method of vaccination against diphtheria to more than 700 school children. No untoward by-effects were noted in any instance, and only occasionally local reactions occurred. Young children and infants gave less local reaction than older children and adults. The intracutaneous method seemed to be the best method of administration. The vaccine is a mixture of toxin and antitoxin, and contains only traces of albumin, so that the danger of anaphylaxis is very slight. Schreiber believes that this method causes a greater production of antibodies than the method of immunization by antitoxin alone. Physicians and nurses frequently exposed to cases of diphtheria gradually become immunized to diphtheria, probably because of repeated mild infections and the consequent increase of antibodies in the blood. The Behring plan of immunization develops a form of active immunity in the same manner.

Salvarsan in Syphilis of the Central Nervous System.—DREYFUS (*Münch. med. Woch.*, 1914, lxi, 525) has used a combination of intravenous injections of salvarsan with mercury and the iodides for the treatment of syphilis of the central nervous system. In some of the cases, details of which are given in the article, very excellent results were obtained. The indications for the treatment are given in detail. Negative findings in the spinal fluid in cerebrospinal syphilis usually indicate that treatment will have no effect. The disease in such cases has become arrested and the symptoms are due to anatomical changes in the cerebrospinal system that cannot be influenced by treatment.

The Mode of Action of Mercury and Salvarsan.—SCHREIBER (*Münch. med. Woch.*, 1914, lxi, 522) is of the opinion that the therapeutic effects of mercury and salvarsan in syphilis can be explained by differing, although complementary, actions upon the virus of syphilis. He bases this belief upon pharmacological and clinical evidence that, according to him, prove that salvarsan kills all the spirochetes it can reach while mercury promotes the immunity reactions. He believes mercury does this by increasing the protective substances in the recipient.

Salvarsan in Syphilis of the Central Nervous System.—IWASCHENZOFF (*Münch. med. Woch.*, 1914, lxi, 530) reports his experiences with the use of salvarsan in 130 cases of various forms of cerebrospinal syphilis. He says that the beneficial effects of salvarsan in such cases is without question. He advises repeated small doses of salvarsan especially

during the early part of the treatment. Initial doses of 0.2 to 0.3 gm. in 100 to 150 c.c. alkaline salt solution were injected intravenously at fourteen-day intervals. In some cases it was possible to increase this dosage, but Iwaschenzoff points out that no definite rules for dosage or contra-indications can be made in the treatment of syphilis of the nervous system. He emphasizes the importance of individualizing the treatment in every case.

The Treatment of Syphilis of the Nervous System by Intrathecal Injections.—CAMPBELL (*British Med. Jour.*, 1914, 2776, 577) says that syphilis is the most common cause of organic disease of the nervous system. When it attacks the central nervous system it gives rise to two sharply differentiated forms of disease, so-called cerebrospinal syphilis and parasyphilis. Campbell prefers to denote these two types of disease as "interstitial" and "parenchymatous" syphilis of the nervous system. Campbell believes that the injection of salvarsanized serum into the spinal canal is the only treatment capable of arresting the pathological process in parenchymatous syphilis. This treatment acts by destroying the spirochetes within the central nervous system and the cerebrospinal fluid. The treatment should be begun as early as possible. Neurons once destroyed are incapable of regeneration. Unfortunately, cases of general paresis and tabes rarely come before us until wide tracts of nervous tissue have been irretrievably damaged. The intrathecal treatment is also indicated in cases of interstitial syphilis, especially of the spinal cord, which do not readily respond to salvarsan, mercury, or iodide of potassium. The latter drug should be given three or four times a day in doses of not less than 60 grains.

Clinical Experiences with Digifolin.—GRABS (*Berlin. klin. Woch.*, 1914, li, 210) has had excellent results with the use of digifolin as a remedy for failure of cardiac compensation. Digifolin may be obtained in tablet or ampoule form, each containing 0.1 gm. of folia digitalis titrate. Digifolin contains the active glucosides of digitalis, but is freed from impurities, especially the safonius and Grabs believes that it is superior to similar preparations derived from digitalis, such as digipuratum and digalen. Grabs found that marked digitalis effect was obtained in cases of mitral cardiac disease, myocardial degeneration and in acute dilatation of the heart. The combination of diuretin and digifolin was very effectual in the more urgent cases with marked dyspnea and edema and in cases complicated with nephritis. Grabs says that no untoward effects follow the administration of digifolin by mouth. After subcutaneous or intramuscular administration, about one-third of the patients complain of slight pain at the site of the injection, but this pain lasts only about an hour. He recommends digifolin because of its stability, the possibility of accurate dosage, its freedom from untoward by-effects and its continued action.

The Palliative Effect of Artificial Pneumothorax in the Treatment of Pulmonary Tuberculosis.—VOORSANGER (*Jour. Amer. Med. Assoc.*, 1914, lxii, 1450) reports 14 cases of pulmonary tuberculosis treated by artificial pneumothorax. Voorsanger believes that those cases should be reserved for artificial pneumothorax which do not respond to the

ordinary methods of treatment. Three of this series of cases were in the advanced stages of the disease. They were selected for lung compression to relieve cough, expectoration, and hemoptysis and not with any hope of arresting the disease. Of the remaining 11, 2 patients could not be inflated, 1 on account of adhesions, the other on account of an old pleurisy with effusion. Three of these cases are arrested, 1 patient is rapidly improving and 4 patients are progressing favorably, being inflated at intervals of four weeks. Two patients stopped the treatment of their own volition. All of the cases were, whenever possible, controlled by roentgenograms before operation and before the second inflation. All compressions were made by the Farlanini method with 0.5 per cent. novocain anesthesia. Voorsanger does not agree with those who assert that this operation should only be performed in a hospital or sanatorium. He believes that, whenever possible, it is better to perform the first inflation at a hospital, but that, when a pneumothorax is once established subsequent inflations are simply and quickly performed.

The Indications and Contra-indications for Digitalis Therapy.—MARTINET (*Presse Méd.*, 1914, xxii, 301) says, contrary to the general belief that increased arterial tension is a contra-indication to the use of digitalis, that digitalis can be used in many cases to lower blood-pressure. When given for this purpose, the remedy should be given in small doses. A lowering of diastolic pressure is first observed but with continued use, the systolic pressure is often also reduced. Martinet has had very good effects by using digitalis intermittently in small doses in the treatment of angina pectoris. His practise is to give digitalin or digalen for periods of ten days followed by intervals of from ten to twenty days. The administration of digitalis in this way decreased the number and severity of the anginal attacks and invariably lowered the diastolic pressure and often diminished the systolic pressure. Much benefit was also derived in cases of hypertension due to cardiorenal sclerosis, but in this type of disease digitalis was given with shorter periods of intermission. Martinet also found that the administration of small doses of digitalis over long periods of time reduced or caused the entire disappearance of attacks of anginal pain in aortic insufficiency.

Clinical Results with Sennatin.—LINDBORN (*Münch. med. Woch.*, 1914, lxi, 872) writes concerning sennatin which was introduced by Credé as a cathartic suitable for subcutaneous or intramuscular use. The average dose is 3 c.c. and no untoward effects have been observed from its subcutaneous or intramuscular use except, in some instances, a transient rise of temperature. Lindborn tried this remedy in 46 patients. He found that it had a distinct effect in increasing peristalsis in 80 per cent. of this series. In 62 per cent. the increased peristalsis was sufficient to produce a movement of the bowels. In 14 of the 46 patients, a single injection of the remedy had a continued action; the patients who formerly never had a movement of the bowels without an enema had spontaneous daily evacuations for periods as long as a week.

OBSTETRICS

UNDER THE CHARGE OF

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Repeated Tubal Gestation with Blood Cyst of the Ovary; Operation; Recovery.—BUTLER-SMYTHE (*Jour. Obs. and Gyn. British Empire*, February, 1914) reports the case of a patient taken with typical signs of ectopic gestation, and operated upon. On opening the abdomen the left tube was much enlarged and the left ovary large and cystic. The patient recovered from the operation, and the specimen consisted of left tubal gestation and a blood cyst of the left ovary. Two years after the patient was taken suddenly ill with symptoms of ectopic gestation with internal hemorrhage. As this had evidently ceased there was delay of twenty-four hours to prepare for operation. When the abdomen was opened a large quantity of dark fluid blood was found and ectopic gestation in the right tube. On examining the specimen the tube showed chorionic villi, the right ovary was a cyst containing dark fluid blood. The patient ultimately made a complete recovery.

Three Atypical Cases of Postpartum Pyelitis.—MURRAY (*Jour. Obs. and Gyn. British Empire*, February, 1914) has treated 8 cases of severe pyelitis commencing after labor. In 5 the diagnosis was easy, with changes in temperature, pus in the urine, and kidney tenderness in 4. In 3 cases there was total absence of local signs and symptoms, temperature remittent rather than intermittent, absence of chills, smaller amount of pus in the urine, although the patients were seriously ill, and the disease beginning on the day following labor. The first case was a primipara with delivery in breech presentation, followed by fever. The urine contained pus and coliform bacteria. The patient gradually recovered. A second case, a primipara, had forceps delivery followed by fever, without signs of uterine infection. The patient had acid urine, 4.5 per cent. of glucose, pus, and coliform bacteria. She died of coma a few days after delivery, and diabetes was thought to complicate the infection by the colon bacillus. The third case, a multipara, gave natural birth to a premature stillborn child. Her symptoms resembled enteric fever with absence of symptoms of streptococcus uterine infection. The blood was negative to the Widal test and culture test for bacillus typhosus. The urine showed the usual signs of colon bacillus infection. A vaccine was prepared from the coliform organism, obtained from the urine, and this produced very steady improvement. In using the vaccine, Murray has found by observation that each patient must be treated individually, and that the dose must be varied in accordance with the nature of the case. In acute pyelitis, a first dose may vary between 3,000,000 and 30,000,000 of autogenous coliform organisms. If no improvement follows such

dose must be rapidly increased at intervals of a day or two until the improvement occurs. The greater the intermissions of temperature, the smaller must be the dose. Where fever was high and continued, 30,000,000 was given as a first dose, increased within two weeks to 250,000,000. Where alkalies or urotropin are used, tests should be made to ascertain whether formalin is really produced. Acid sodium phosphate in half dram doses, three times daily should be given. Urotropin should be given in tablet or powder alone. After a preliminary small dose as a test this drug should be pushed to 20 or 25 grains, three times daily.

The Treatment of Eclampsia by Euphyllin.—LICHTENSTEIN (*Zentralbl. f. Gyn.*, No. 23, 1914) states that he has obtained good results by the employment of euphyllin. This substance is a combination of theophyllin and ethylendiamin. It is 40 per cent. soluble in water and contains 78 per cent. theophyllin. Its solubility makes it very adaptable for injection and it works promptly and efficiently. In 5 cases of eclampsia where the secretion of urine was almost suspended, this substance injected into the muscles in doses of 2 c.c. produced great increase in the diuresis.

Uncontrollable Uterine Hemorrhage.—In the *Jour. Obs. and Gyn. British Empire*, March, 1914, BRIGGS AND HENDRY contribute an interesting paper, giving the results in the examination of 104 uteri removed by hysterectomy for uncontrollable bleeding. The writers conclude that uncontrollable uterine hemorrhage is a functional disturbance; the disturbers local and general, numerous and varied. Among them, arteriosclerosis, fibrosis uteri, chronic metritis, and chronic infective endometritis have been rated too highly and considered too important in pathological treatment. For two or three weeks after an early abortion, curettage may remove successfully the friable relics of conception, but in other cases the use of the curette fails, and many erroneous diagnoses of endometritis result. In both treatment and exploration curettage is uncertain in success and failure. Chronic appendicitis with growths in the uterus, and retention of growths of conception may cause uncontrollable bleeding, when the uterus itself is not at fault. The real pathology of cases is often obscure, as a case where hemorrhage at menstruation has been increasingly great, after a brief period of amenorrhea, followed by an unrecognized case of early abortion, is diagnosticated as a case of metrorrhagia. Examination may show a small placental polyp is present. The case becomes clearer if one remembers that in this particular instance the average abortion rate, 15 to 17 per cent., had not been exceeded, and that sterility occurring usually in 5 of 95 married women, was below the average rate. The paper is accompanied by illustrations.

Chorio-epithelioma with Difficulty of Diagnosis.—WILLIAMSON AND NOON (*Jour. Obs. and Gyn. British Empire*, March, 1914) report the case of a multipara who expelled a vesicular mole after three months of amenorrhea. A month after she had fever and abdominal pain, and six weeks after the expulsion of the mole an abscess was opened and drained through the vagina. Four months later she was well.

About a year after, menstruation ceased and she was taken with sudden abdominal pain, loss of appetite, vomiting, constipation, and loss of weight. After some weeks she coughed up frothy, blood-stained mucus. On admission to hospital the patient was jaundiced, the tongue furred and dry, temperature 99° F., pulse 108, respirations 40. The breathing was shallow, the left side of the chest moved imperfectly, percussion was dull, and breath sounds weak over the left lung. The lower abdomen was distended. A tumor extended out of the pelvis seven inches above the pubes, and very clear soufflé could be heard over its right upper border. The tumor was elastic, slightly tender, and not fixed. Liver dulness seemed normal. On vaginal examination there was a round, tender, elastic mass in the pelvis, from which the uterus could not be separated. The cervix was high up behind the symphysis, the tumor encroached upon the bowel, the urine contained bile, and the blood examination showed 3,500,000 red and 10,000 white cells. x-ray examination showed dark areas indicating deposits in both lungs. Abderhalden test was then applied for both pregnancy and carcinoma, with placental tissue. The result was strongly positive by the ninhydrin test and the optical method. With carcinoma tissue the result was negative, and diagnosis of chorio-epithelioma was made. Twenty days after admission the patient died with failure of respiration. Autopsy confirmed the diagnosis.

The Practical Relation between Maternal and Fetal Blood.—VOLLHARDY (*Zentralbl. f. Gyn.*, 1914, No. 20) has studied the blood from the mother and from the umbilical cord to ascertain the difference between them, and what test gives a practical result. He finds that the test with acids or platinum chloride shows a marked difference between these two substances and that this can be applied to the dry blood. Fetal blood may be recognized as giving a negative reaction to the test even when an alcoholic extract of the blood has been made. The Abderhalden method was tried and was found unreliable.

The Final Results of Ectopic Pregnancy.—SMITH (*Surg., Gyn., and Obst.*, June, 1914) has studied the results obtained in 192 cases operated upon for ectopic pregnancy, and their condition five years after operation. He finds that in 145 cases the general health is described as good. The final result then, so far as the general condition of the patient is concerned, was very satisfactory. In 144 cases in whom pregnancy might have occurred after the operation, 97 remained sterile. As regards the recurrence of ectopic pregnancy, of the 192, 48 had abortions or were in such condition that recurrent ectopic pregnancy could not take place. Of the 144 in whom pregnancy could happen, 47 had uterine pregnancies, 42 with living children, 64 children in all; 1 stillbirth, 5 aborting without children, 5 abortions and children. Among these there were 21 cases of repeated ectopic pregnancy, half as many as had living children; 2 of these patients had subsequent children and also ectopic pregnancy. Of the 67 women aged under thirty years, 27 had subsequent uterine pregnancies, of whom 10 had repeated ectopic pregnancy. Of the 74 women aged above 30 years 19 had subsequent uterine pregnancy and 11 had repeated ectopic pregnancy.

Essen-Möller finds 46 per cent. of patients operated upon for ectopic

pregnancy, have children subsequently. Prochownik 43.8 per cent., Smith 32.6 per cent., and of these in Smith's series 14.6 per cent. had repeated ectopic pregnancy. Under these circumstances, when operating upon a case of ectopic pregnancy of tubal origin, should the opposite tube be left? To do this certainly exposes the patient to the possible risk of repeated ectopic pregnancy, and yet to remove both tubes destroys the possibility of pregnancy. Smith believes that the age and general strength of the patient, her circumstances and her own convictions in the matter must be carefully considered. In some cases it is far wiser to remove both tubes, in others this should not be done.

The Abderhalden Test for Pregnancy.—WALLIS (*Jour. Obs. and Gyn. British Empire*, February, 1914) reviews extensively the literature upon this subject. He adds his own experience in testing the sera of 50 women known to be pregnant. Of these, 20 were in the last three months, or had recently been delivered. In each case the optical test and the test by dialysis were positive. The remaining 30 were in the earlier months of pregnancy, from the eighth week to the fourth month, and gave a positive reaction. In 30 non-pregnant women the reaction was negative to both tests; 8 of these patients had cancer and 14 syphilis. The sera of 30 males were tested by both methods, with negative results. A large number of these men had syphilis. In 110 cases the test was correct. In 8 cases the sera of patients with cancer digested cancer tissue, but did not digest placental tissue. The sera of 5 cases with tuberculosis were tested with emulsion of human tubercle bacilli with positive results. One case of tuberculous salpingitis gave a positive reaction with the emulsion, a negative with placental tissue. The controlled sera in 10 cases gave negative results to tubercle, including one case of hydrosalpinx, found at operation not tubercular. Repeated attempts to use the test in the diagnosis of syphilis have failed. In 18 cases with various complications the test was made and the optical method was correct in each; 3 had suspected ectopic gestation; 6 had tumors where pregnancy in addition was suspected; 3 had chorio-epithelioma, 1 cholera, 1 heart disease with amenorrhea, 2 nephritis, 2 puerperal sepsis. In 2 cases of inflammation of the tubes the test by dialysis failed; no optical test was made. The test is essentially for the presence of chorionic villi, and will be positive so long as these remain in the body of the patient in contact with her blood. There will probably be valuable aid given by this test in studying the toxemias of pregnancy and the ferments formed by the liver and kidneys. At present Wallis believes that it has been fairly established that the serum of pregnant women contains a specific ferment capable of digesting placental tissue, and this ferment can be detected from the eighth week of pregnancy until ten days after delivery by the optical and dialysis methods. Both tests should be used in the case and the accuracy of the results obtained by the most scrupulous care in details of the method. These tests are of value in diagnosis in the early diagnosis of pregnancy; the differential diagnosis between fibromyomas and pregnancy, the diagnosis of ectopic gestation, of chorio-epithelioma, and retained placenta. At present there is no reason for believing that the serum of pregnant women will digest other than placental tissue.

GYNECOLOGY

UNDER THE CHARGE OF

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Pathology and Treatment of Chronic Leucorrhea.—In a continuation of the work reviewed in this department a few months ago, CURTIS (*Surg., Gyn., and Obst.*, 1914, xix, 25) gives some of his deductions as to the etiology and best methods of treatment of leucorrheal discharges. He believes that in the vast majority of cases, vaginal discharge in a non-parous woman is of gonorrheal origin, even if the gonococcus be no longer demonstrable by any known method; in women who have borne children, however, other factors come into play, such as altered anatomical relations, loss in elasticity of the tissues, etc., so that the gonococcus cannot always be held responsible. As was stated in the previous paper, the author firmly believes that the usual seat for the formation of purulent discharges is the lower genital tract (lower cervix, vagina, vulva), the endometrium remaining uninvolved. The indications for treatment he resolves into the following categories: (1) Improvement of the lowered resistance of the genitalia, which often exists, by improving the general health of the patient, proper attention to the bowels, repair of any lacerations present, correction of displacements, etc. (2) Avoidance of measures which are not only useless but often harmful; among these Curtis classing curettement, douches, and tampons. (3) Reduction of the mucous discharge from the cervix, since this forms an excellent culture medium for any bacteria present, and thereby plays an important role in the production of leucorrhea. While theoretically operation, with actual excision of all glandular tissue, might be advisable, scarification, or the repeated application of strong silver nitrate (20 per cent. solution) to the cervical canal, have proved satisfactory measures in most cases. (4) Application of the same solution to urethral granulations, Skene's and Bartholin's glands, or the excision of the latter, to remove thoroughly all residual gonococci. (5) Vaccine and powder treatment; vaccine therapy was given a thorough trial, autogenous vaccines, made from what appeared in each individual case to be the predominating organism or organisms, being used; in many instances these were of the anaërobic group. Injection was started with low doses—10,000,000 to 20,000,000—and rapidly increased to from 150,000,000 to 300,000,000 at a time. While the results in a number of patients appeared favorable at first, as a rule the symptoms subsequently recurred and were then apparently uninfluenced by treatment. A thorough trial was also made of a large number of the various drying powders and yeast preparations, so strongly advocated by the Germans, with again irregular, and on the whole, disappointing results. Temporary improvement was the rule, irritation and discharge lessening during treatment, but only to recur in many instances upon its cessation.

Massage Treatment of Pelvic Inflammations.—In an article entitled "Twenty Years of Gynecological Massage," DELASSUS (*La Gynecologie*, 1914, xviii, 81) makes a strong plea for a more careful consideration on the part of the profession of this form of physiotherapy, which he says he is convinced, after many years' experience with it, often is able to replace operation, and to restore more or less invalid women to a condition of functional health. He claims no particular originality for what he has to say, but merely wishes to point out some of the essential details, the ignorance or non-observance of which has often led to disappointing results, and therefore to disgust with the entire method. The only apparatus required for the proper application of gynecological massage is a fairly firm table or couch, of sufficient height to permit the operator to reach the patient without discomfort. Upon this the patient lies in the dorsal position, with the knees drawn up, and the clothing sufficiently loosened about the body to permit of free access to the abdominal wall; it is well to place a small pillow under her head and another under the lower part of the spine. Standing at the left side of the patient the physician gently introduces the index finger of his left hand into the vagina; this serves merely for support and counter-pressure in the subsequent manipulations, which are in most cases carried out entirely by the right hand placed upon the abdomen. At first only very gentle manipulations—pressure along the muscles, superficial strokings, tapplings, rubbing, etc.—should be made, at a distance from the site of the chief lesion, just as one would massage at first gently around an inflamed joint or a fracture. Later, deeper pressure may be made, but throughout all semblance of violence is to be rigorously avoided. If much pain is caused it indicates either that the lesion is still too acute and the treatment should be postponed, or if the lesion is chronic that this form of therapy is contra-indicated. The author emphasizes the fact that patience is the key-note in the successful application of this treatment, and is required of both doctor and patient. The chief difficulty met with at first is usually the resistance of the abdominal muscles; even with the best of will, the patient is often unable to overcome this. No attempt should be made to conquer by force, but rather by gradually distracting the patient's attention and winning her confidence. Each seance should last at first about five to six minutes, gradually increasing up to a quarter of an hour. The best results are obtained if treatments are given daily, though often this is impossible; they should under no circumstances be farther apart than three times a week, however. *Indications:* The author is distinctly conservative in this respect, and does not attempt to draw all forms of gynecological disease into the realm of massage therapy. He gives the following as the type of case *par excellence* in which it is indicated: A young woman (twenty to thirty-five years) who has had two or three children, or several miscarriages, who now complains of irregular and painful menstruation, moderate leucorrhea, indefinite pains in the groins and lower abdomen, and a feeling of heaviness and general malaise; is nervous, irritable, upset at the least little domestic worry, and generally below par. Such patients, upon examination, are usually found to be exceedingly tender to vaginal pressure, even before the adnexa are reached; the latter are slightly enlarged and very tender to bimanual palpation. The condition,

an exceedingly common one, is a chronic salpingo-oöphoritis with pelvic cellulitis. The first effect generally noted from massage treatment in such a patient is a relief of the heavy feeling in the abdomen, then gradual disappearance of the pains and tenderness, reëstablishment of regular and painless menstruation, often relief of dyspareunia, etc. In starting a course of treatment, however, no definite promises should be made, and unless distinct pain is caused, or the patient is getting worse, it should be tried for at least two weeks before forming any judgment as to its efficacy; if improvement is noted it should then be continued until a definite cure is attained or a status quo is reached, beyond which no further progress is made. Delassus believes that in most instances the cure is symptomatic, rather than a true return of the diseased organs to a normal anatomical condition, but he reports one case of a woman who was sterile for thirteen years after the birth of her first child, but who became normally pregnant some months after undergoing massage treatment, and another instance in which a woman who had had five successive miscarriages at about the second month was enabled to go to full term, indicating at least that a functional *restitutio ad integrum* may occur. In some instances the symptomatic cure is apparently permanent; in others recurrence takes place, and further series of treatments become necessary or operation may be indicated. The author admits that he cannot give a scientific explanation for the results obtained, but suggests that they may be due to an emptying of congested bloodvessels, excitation of vasomotor centres, and consequent relief of edema and congestion.

Conservative Surgery of Benign Ovarian Tumors.—FREUND (*Zentralbl. f. Gyn.*, 1914, xxxviii, 985) has devised a method for the preservation of some functioning tissue in operating for even quite large tumors or cysts of the ovaries in cases where this seems especially desirable. Although many operators have practised to a greater or less extent partial resection of the ovaries under certain circumstances, they have for the most part limited the application of this process to small growths or inflammatory conditions, and have generally been content with preserving a portion of the hilus, believing that any functioning ovarian tissue left is most apt to be situated in this region. Freund has found, however, that while this generally holds true it by no means always does so, some cysts, for instance, developing in the hilus, and pushing the only bit of undestroyed ovarian tissue to the farthest pole, or some other portion of the surface of the tumor. In such cases, therefore, as appear suitable for conservative surgery, Freund proceeds as follows: After opening the abdomen the entire or partially evacuated tumor (cyst) is delivered through the incision and completely packed off from the abdominal cavity. The tumor is then bisected throughout its extent, the pedicle being grasped in the left hand. After the contents are thus evacuated every point of the wall can be quickly examined by the eye and finger, and any remaining area of normal ovarian tissue quickly localized. If this is found near the pedicle the tumor is simply cut away in such a manner that the tissue to be preserved is left in contact with the pedicle, which is then sewed over with a fine suture. If the ovarian tissue is on the periphery of the tumor, however, a thin strip of tumor capsule is left between the pedicle and the ovarian remnant;

thus the latter is maintained, while the growth is completely removed. It is, of course, important that the ovarian artery shall not be tied, but this is not necessary, as the hemorrhage is generally very slight. The chief indications for this operation are found in cases of bilateral benign growths, such as pseudomucinous cystomas, follicular and corpus luteum cysts, and dermoids occurring in young women. The author reports that in all cases upon which he has performed it (running back over three and one-half years) menstruation was preserved and no signs of the artificial menopause occurred. As yet he is unable to report the subsequent occurrence of pregnancy, but hopes to be able to do so in the future.

OPHTHALMOLOGY

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Paralyses of the Motor Oculi in Otitis and Sinusitis.—BERARD, SARGNON AND BESSIERE (*La Clin. Ophtal.*, December 10, 1913, p. 698) find that isolated complete paralysis of the third nerve in chronic otitis is extremely rare compared with the much greater frequency of isolated paralysis of the external rectus described by Gradenigo. Besides a lesion of compression in cerebral abscess, isolated and complete paralysis of the motor oculi may be due to a lesion of the anterior part of the petrous, and especially of the external wall of the cavernous sinus. Intervention may be attempted, but the prognosis is very grave. In the course of frontal, ethmoidal, sphenoidal, and even maxillary sinusitis, isolated partial or total paralysis of the third nerve may occur; the partial variety is of favorable prognosis, but the total form is much graver; the latter may, however, recover, sometimes even spontaneously.

Treatment of Squint.—v. GROSZ, in an address before the Belgian Society of Ophthalmology (*Klin. Monatsbl. f. Augenhk.*, September, 1913, p. 424), advocates commencing treatment at the earliest age by the continued instillation for several months, in both eyes alternately, under constant medical control of a 1 per cent. solution of atropin. With intelligent children stereoscopic exercises should be begun early. The wearing of properly correcting glasses is of importance. As regards operation, there is no need for haste, unless for special reasons it may be delayed until the eighth or tenth year. In many cases of convergent strabismus, particularly the alternating form, simple tenotomy will be sufficient. The author does not agree with the view that this operation may be dispensed with or that it is injurious. In divergent stra-

bismus, where the deviating eye is, as a rule, amblyopic, tenotomy is of little service and advancement is to be preferred. In the discussion, de Lapersonne (Paris) shared the view that operation should not be performed in convergent strabismus before the tenth year. He likewise has not abandoned tenotomy, although he regards advancement as holding the first place. Following operation binocular vision is frequently remarkably improved and can be further developed with the diploscope. Jessop (London) likewise does not operate before the tenth year and performs advancements only and highly values alternate atropinization in young squinters.

Hypophysis Tumors.—FLEISCHER (*Klin. Monatsbl. f. Augenhk.*, vol. lii, p. 625), from an analysis of fifteen cases, finds that visual disturbance when once begun almost invariably led to blindness in the course of a few years. Hemianopic temporal defects were present in every instance. Two cases operated by Schlöffer's method and one by von Hirsch's ran an extremely favorable course. In one case there were no further morbid phenomena, and the patient was able to return to work, as was also the fact in a second case. In a third the nasal half of the field was recovered. Operation is accordingly to be insisted upon, especially if there is provisional loss of visual acuity.

Treatment of Luxations of the Crystalline Lens.—ASK (*Klin. Monatsblatt. f. Augenhk.*, September, 1913, p. 331), based upon pathological, anatomical, and clinical experience, argues that the intrabulbar luxated lens constitutes a permanent threatening danger for the eye and should accordingly be removed whenever possible. He especially insists that his own pathologico-anatomical findings in subconjunctival luxations urgently bespeak early operation (enucleation if necessary, and this with regard to the danger of sympathetic ophthalmia; otherwise, as a rule, early removal of the subconjunctivally luxated lens) and against the views of Stellwag, Manz, and Mackenzie, which are still prevalent today, that to favor consolidation of the scleral cicatrix extraction of the subconjunctivally luxated lens should be postponed for a considerable period.

Fibrolysin in Stricture of the Lacrymal Canal.—WOLFFBERG (*Woch. f. Therap. u. Hyg.*, 1913, No. 44, p. 398) confirms the statement of P. Colin regarding the beneficial action of injections of fibrolysin. He has treated satisfactorily ten cases of blennorrhoea of the lacrymal sac with strictures impervious to the smallest probes. After thorough cleansing with hydrogen peroxide he injects with the Anel syringe a little suprarenal-cocaine solution, following which a few drops of fibrolysin are deposited in the same manner upon the strictured point. In a quarter of an hour in one case reported a probe could be introduced and passed smoothly the following day. Fourteen days' treatment resulted in cure. The writer particularly emphasizes the rapidity of action of this medicament.

The Eye-ground in Psychoses.—BENEDICT (*Annals of Ophthalm.*, April, 1914, p. 233), from a study of the fundi of psychopathic subjects, concludes (1) that well-defined disorders from extensive morbid con-

ditions may exist for sometime without change in the ophthalmoscopic appearances of the eye-grounds; (2) cases of dementia precox, either slowly developing or rapidly deteriorating, present no associated disk changes peculiar to this condition, but rather a higher percentage of normal fundi than either the organic or functional group of psychoses; (3) in functional psychoses there is no definite association between the mental disorder and the ophthalmoscopic appearance of the fundus.

The Scientific Basis of Potassium Iodide in Arteriosclerosis.—FLURY (*Archiv. of Ophthalm.*, July, 1914, p. 405) summarizes the results of experimental investigation as follows: The drug has a pronounced salt action, whereby it modifies osmotic processes and increases cellular activity. In addition the specific effect of the ions must be regarded. The potassium by its action on the central nervous system and muscles facilitates the transport of the salt in the tissues and the exchange of ions, and also causes special changes in the mineral metabolism. The peculiar distribution of iodine in the body shows that it has a distinct affinity for certain tissues. As regards arteriosclerosis, the arterial vessels as well as the glandular cells and many diseased tissues are able to collect iodine. The therapeutic use of iodide of potash may not only influence metabolism, but directly affect the vascular elements in arteriosclerosis. The reduction of the friction of the blood which potassium iodide causes may result in an improvement in the circulation and increased diapedesis. It may also be assumed, from the known effects of poisoning with iodine in man, that the reduction of blood-pressure plays a role in the action of the remedy. Iodide of potash cannot be replaced by any other salt or any of the numerous modern substitutes, inasmuch as its therapeutic effect depends upon the salt, the potassium and the iodine, of which the latter is probably the most important.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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How Salivary Secretion is Influenced.—WERTHEIMER and BATTEZ (*Jour. de Physiol. et de Path. Gén.*, November 15, 1913, vol. xv, No. 6) have undertaken experiments to decide the question of how the salivary glands are stimulated to secretion. It will be remembered that Cohnheim and Lichtheim found that salivary secretion increased if saline solution was introduced into the circulation. They considered that salivary secretion was one means by which the body cleared itself of the excess of fluid. Later Cohnheim found that even

without the assistance of the secretory nerves a hydremic condition led to an increase of the secretion, and sometimes to a distention and edema of the glands, and thought that these manifestations were entirely separate from the nervous system; he went further, and having paralyzed the chorda tympani by atropin, he still found that injection of saline was efficient in producing edema of the gland. Hamburger considered that there could be no salivary secretion without nervous excitation, and thought that the reason why solutions of certain salts caused salivation was by the eliminated salts impressing the gustatory nerves. The authors think that gustatory excitation plays no part in the provocation of salivary secretion by the injection of salts, for after section or paralysis of the gustatory nerves, as well as after the injection of pure and distilled water, the salivation was obtained. They consider that the reactions of the submaxillary gland, either intact or deprived of its nerves, show that the secretion following transfusion of liquids into the blood is almost entirely under control of the central nervous system excited directly by the heightened blood-pressure. Such excitation they consider is transmitted by the chorda tympani. Compression of the abdominal aorta, which increases the pressure in the subdiaphragmatic region, has the same result, although less marked, as follows the injection of saline, especially in animals whose blood is already in a hydramic state.

Carrot-juice Agar as a Medium.—ROCHAIX (*Jour. de Physiol. et de Path. Gén.*, November 15, 1913, vol. xv. No. 6) finds that carrot-juice agar is an extremely useful medium for the growth of colon, typhoid, and paratyphoid of many sorts, of which it gives abundant cultures in twenty-four hours at 37°. It is equally applicable to *Bacillus pyocyaneus*, anthrax, *Streptococcus pyogenes*, and the encapsulated group, while, on the contrary, it is unfavorable to the development of staphylococcus, diphtheria, and pneumococcus. It is made as follows: carrots well washed are cut up and the juice expressed; 200 c.c. water is added to 800 c.c. of carrot juice, and agar is added, as in the preparation of ordinary peptone jelly, in the proportion of about 30 to 35 grams per 1000 c.c. The mixture is kept at 115° for twenty-five minutes in the autoclave; clarified with white of egg; alkalinized, and filtered. After being tubed it is sterilized again at 108° to 110°, after which the medium is more clear and transparent than the ordinary peptone jelly. The author has used also carrot juice, agar glycerinated, artichoke agar, potato agar, and beet-root agar, but finds that, everything considered, the first named is the best, for the reason that with simple economical preparation and absence of peptone it is yet possible to obtain luxuriant growths of the bacilli indicated, and very rapid growths of molds; while the production or absence of gas in the agar cultures is another differential characteristic which can be added to those already known as separating the colon-typhoid group from the encapsulated forms.

The Frequency of Tuberculosis.—LUBARSCH (*Vireh. Arch.*, 213, 417) publishes autopsy figures which are authoritative from Posen, Zurekau, and Düsseldorf, showing that tuberculosis was present in 57.4 per cent. of 7371 cases, whereas it was found in 69.2 per cent. of 5800 adolescents.

Orth adds as a footnote that 51.4 per cent. was the figure for his own institute (1000 autopsies in Montreal gave a total tuberculosis figure of 43.7 per cent.). Since the figures for latent and healed tuberculosis were higher in adolescents than in all cases, the conclusion appears to be justified that the tendency to healing and to a harmless course is greater in the former. Further, in 1114 cases Lubarsch was able to determine a hematogenous source for 29 per cent.

Plasma Cells in the Kidney.—CEELEN (*Virch. Arch.*, 211, S. 276, 1913) has examined a series of 60 kidneys, mostly from the young, some from the newborn. His contention is that plasma cells are never found in the normal kidneys, and nearly always in the damaged organ, save perhaps in cases of simple hyperemia; in pyelonephritis they are likely to be especially prominent, and they may be so numerous in interstitial nephritis as to merit the statement that in primary interstitial nephritis (if one allow the term) there is a plasma-cell stage. The cells are found in the periphery of the veins and arteries and above the Malpighian bodies. They vary greatly in size and may be multinucleate. They are histiogenous, originating from the capillary endothelium, from adventitious cells, but probably not from hematogenous lymphocytes. They may give origin to smaller round, plasma daughter-cells. They may be found in the blood; they give us specific indication of disease, save that in the newborn they are characteristic of syphilis.

An Unusual Form of Meningeal Tuberculosis.—VON CZIRER (*Centralbl. f. allg. Path. u. path. Anat.*, Bd. xxv, No. 4, 28, February, 1914) describes a very unusual form of meningeal tuberculosis which occurred in a man aged twenty-five years; a flattened, outspread mass of pale reddish-gray color and 0.5 cm. thick lay over the convexity of the left hemisphere. It measured 8.5 by 5.7 cm., and broadened out over the posterior part of the frontal lobe and the front part of the parietal. Macroscopically it was judged to be a sarcoma, but its microscopic examination determined a tuberculous character, and the specific bacilli were found in the sections. It is very unusual to find a departure from the usual basal inflammation, and Czirer has found only two or three cases reported.

Market Butter.—In a study of the market butter of Boston by ROSENAU, FROST, and BRYANT (*Jour. Med. Res.*, March, 1914) there are one or two points of interest to the casual reader. All the specimens tested would be classed as good butter, and, it may be remarked in passing, passed the necessary standards. Twenty-five samples averaged five and a half million bacteria per gram, and the authors state that the bacteria diminish markedly with age of the butter in which they are contained. One sample diminished 85 per cent. in two weeks, two others over 90 per cent. in four and six weeks. *Bacillus coli* appeared occasionally, streptococci frequently, and *B. welchii* not at all, although this last is frequent in milk. Tubercle bacilli were found in two of twenty-one samples, which gives a figure corresponding closely to the number of milk samples similarly inspected. The authors consider that the cream used for butter should be pasteurized, the

more so as general high quality of butter is no guaranty of safety in this regard; the samples which contained tubercle bacilli were, in fact, the most high-priced and generally excellent samples in other regards.

The Eosinophilic Granules.—MILLER (*Centralbl. f. allg. Path. u. path. Anat.*, Bd. 25, No. 6, March 31, 1914) takes up the ill-understood subject of the natures of the eosinophilic granules. He is strongly opposed to the idea that these originate from hemoglobin or are of hemoglobin nature; they are to be found in low forms of life which possess no red corpuscles, they contain no hematin group; a change of fragments of erythrocytes into these granules has never been observed, and eosinophiles do not give origin to pigment cells; even staining differences are to be observed between these and hemoglobin particles. The granules, moreover, are in direct connection with the stroma of the cells. Nor, thinks the author, are these granules of the nature of the bodies known as Russell's fuchsin bodies, which are found very exceptionally in plasma cells. Miller considers that the presence of eosinophiles has no diagnostic value in the differential diagnosis of gonorrheal disease of the adnexa.

Salvarsan and Other Therapeutic Agents as Antiseptics.—SCHIEMANN AND ISHIWARA (*Zeits. f. Hyg. u. Infektionskr.*, Bd. 77, Hft. 1, 1914) have conducted painstaking labor upon the antiseptic qualities of salvarsan and ethylhydrocuprein, and they find that *in vitro* these agents prevent growth in dilutions of one in a million. The actual killing power of salvarsan exists in such dilution, but is excited slowly so that at the end of twenty-four hours the height of the action may not be reacted. The drugs are selective, also, salvarsan being effective on the anthrax, glanders, and erysipelas organism, cuprein on pneumococcus, the effect on various other bacteria being lessened a hundred and even a thousand fold. In serum, the effects are not greatly different from those observed in bouillon, activated serum permitting a greater effect than inactivated, which is the opposite result to that found in the case of sublimate. Phenol is weakened by serum to a less degree than is sublimate. The effect of salvarsan differs according to the kind of serum, cattle serum giving a less potent result than rabbit serum. The authors explain the differences seen in salvarsan and cuprein on the one hand, and sublimate on the other, as the result of the lipoids in the serum. Lecithin and cholesterin added in a strength of 1 in 100 caused a very marked weakening of the ability to prevent growth of bacteria.

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ORIGINAL ARTICLES

THE CLINICAL VALUE OF EXPECTORANTS.

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THE medical literature does not contain, so far as I have been able to determine, any accurate bedside observation on the value of expectorants. There are many references of medical men's impressions, but nowhere carefully recorded facts that will bear close scrutiny. When an investigation of this subject was first considered, after reviewing the literature, several methods were considered and tried for an accurate bedside study of the subject. It was impossible, however, to obtain satisfactory data, so this was abandoned and the work carried on with the laboratory animal; and it would appear that an accurate bedside study of the action of expectorants offers at present insurmountable difficulties. Patients with acute bronchial troubles are unsuited for study on account of the rapid and marked spontaneous changes that may occur. Those with chronic bronchitis, where the daily or even weekly variations are imperceptible, are most suited for a study of this character. In these patients, however, it is apparently impossible to determine accurately the amount and viscosity of the sputum. The admixture of saliva and the length of time the secretion has remained in the trachea or bronchi, with consequent loss of water, must all be considered.

The review of the literature is comparatively simple, as the total published information upon this subject, outside of that contained in the text-books on pharmacology, is confined to less than a half dozen monographs. The total evidence at hand, therefore, consists of purely theoretical consideration and three or four

series of observations performed upon laboratory animals, to which we have added some additional laboratory experiments.

Expectorants may be defined as agents which facilitate the removal of secretion from the air passages. Several factors play a role in this process. The act of coughing, by increasing air currents, carries upward the secretion in the trachea and larger bronchial tubes, but has no effect upon the bronchioles. In these latter the chief factor is the ciliary movements of the bronchial mucosa. It has been determined by Gebhart, Henderson and Taylor, and others that the ciliary activity is capable of carrying mucus 1.5 to 2.5 cm. per minute. Increased viscosity of the mucus interferes materially with this movement, and Engelmann has shown that it may entirely inhibit the action of the cilia. The third factor is the presence in the alveoli and smaller bronchioles of a peristaltic-like movement; this probably under vague control (Einthoven, Sandimann). These movements somewhat resembling intestinal peristalsis, are probably important factors in removing the mucus from the alveoli and terminal bronchioles, neither of which are provided with cilia. To facilitate removal of mucus it would, therefore, be necessary to stimulate coughing, increase the ciliary movements, lessen the viscosity of the secretion, or stimulate bronchial peristalsis.

The cilia are not supplied with nerves, and it is therefore impossible to stimulate them through the nervous system. Virchow, in 1854, demonstrated that the direct application of weak alkalies increased the activity of the cilia, and Rossbach claimed that alkalies by the mouth had the same effect. Cushney states that alkalies are not secreted through the bronchial mucosa, and certainly in the ordinary doses the amount so secreted must be negligible. It is, therefore, highly improbable that any of the expectorants increase the ciliary movement.

There is no evidence that any of the expectorants increase the rhythmical muscular contraction in the bronchioles. It is possible that apomorphin in large doses may stimulate the vagus and thus increase peristalsis.

The final possibility is the action of expectorants in thinning the bronchial secretion. The trachea and bronchi are richly supplied with mucous glands capable of producing a profuse secretion. The viscosity of this secretion may be lessened either by increasing the amount of secretion or by introducing into the secretion something which would dissolve the mucus, as for instance an alkali.

The expectorant action of ammonium chloride and ammonium carbonate was thought to be due to their elimination through the bronchial mucosa, the alkali thinning the secretion. This theory, however, will not bear close scrutiny. Biedl, Winterberg, and others have shown that one-half to four-fifths of the ammonia administered disappears in the liver, never reaching the systemic

circulation. In the ordinary therapeutic dose of 0.3 gm. no more than 0.15 gm., or 2.5 grains, would reach the general circulation, and at most only a small part of this would be excreted by the bronchial mucosa, an amount certainly too small to modify the viscosity of the mucus. In case, therefore, the ammonium salts mentioned thin the mucous secretion they must act through some different channel. It is now believed that their action is upon the bronchial gland centre, which, in its activity, apparently shows a parallelism with the salivary centre. It is thought that the centre may be stimulated either directly by substances in the blood or reflexly from the stomach and mouth. Biedl and Winterberg have shown that in order to stimulate this centre in dogs it requires 2 to 2.5 mg. of ammonium salts per 100 gm. of blood. They found that when injected intravenously into a 7 kilo dog 0.48 gm. of ammonium chloride was required, and if given by the mouth twice this amount, equivalent to about 9 gm. in a man.

Turning to a consideration of the experimental work performed with ammonium salts, Rossbach, in 1882, endeavored to determine the amount of tracheal secretion in cats by exposing the interior of the trachea by means of a longitudinal slit and then observing the secretion directly. The exposed mucosa was dried with filter paper and the time noted in which secretion occurred. Drugs were then given and the secreting time again observed. He used large doses of ammonium carbonate, 2 gm. intravenously, and reported a definite delay in the secretion time. He also failed to increase secretion by painting the mucosa with a 1 per cent. solution of ammonium carbonate.

Calvert, in 1896, repeated Rossbach's experiments with quite different results. He refers to only two experiments, both on cats. He reports that after the intravenous injection of 2 gm. of sodium carbonate there was a shortening of the secretory time of one minute. Considering the method employed, namely, the covering of a previously dried surface with a secretion, this difference in time is too slight to enable us to draw any conclusions. Henderson and Taylor call attention to the late appearance of the secretion in one of Calvert's cases, thirty-seven minutes, as after an intravenous injection the effect should be noted within ten or twenty minutes. The possibility of such a surface being moistened by secretion carried up from below by the cilia makes another probable source of error.

Henderson and Taylor, in 1910, studied the action of expectorants by the following method: Cats were anesthetized with chloroform or ether, or both. This was followed by urethane, which kept the animal asleep during the period of observation. One limb of a Y-tube was fastened into the trachea, another to a calcium U-tube and the other limb to the blast side of a Meyer respiratory pump, the exhaust end of which was attached to the other end of the calcium

U-tube. The animal was placed upon its belly on an incline to assist in the escape of mucus. By this method not only the mucus but the water also contained in the expired air was estimated. This latter factor apparently introduces an element of error, as they found it varied with the temperature of the animal, the amount of air forced into the lung, and the state of the animal's circulation. They reported that ammonium carbonate or ammonium chloride in large doses given intravenously equivalent to 12 gm. for a 70 kilo man, caused marked increased secretion of mucus. Two and a half times this dose, an equivalent of 30 gm. for a man, given by the mouth, also caused increased secretion. Doses of 40 mg. of ammonium carbonate intravenously, equivalent to 1 gm. in man, at times failed to produce any increased secretion. In one instance 50 mg. of ammonium chloride intravenously, equivalent to 1.25 gm. in man, failed to increase secretion. The dosage with which they obtained results was far in excess of that usually employed by the clinician, and therefore it may be said that they have not shown that in man these drugs in the ordinary therapeutic dose acts as expectorants. When they obtained results the increased secretion appeared in about ten minutes and was transitory in character, rarely lasting more than twenty minutes.

On account of the conflicting reports upon the action of the ammonium salts on bronchial secretion the following experimental work was carried out. Oblong pieces of filter paper of uniform weight and size, 6x12 cm., were rolled in such a manner so as to fit into the trachea and still leave a lumen of about 1 cm. Dogs averaging about 7 kilos were anesthetized by giving 5 gm. of chloretone in alcohol. The trachea was then severed transversely, just below the larynx, all bleeding stopped by means of the cautery, and a weighed rolled filter paper introduced. This came in close contact with the mucosa for a distance of about 6 cm. Such a filter was left in place ten minutes, then reweighed, and the increase taken as an index of the amount of secretion from the mucosa. This should also include some of the moisture in the expired air and mucus carried up from below. After two control readings of ten minutes each the ammonium carbonate in moderate doses was injected directly into the duodenum, and then another series of readings was taken, each of ten minutes, and continued for thirty minutes or more. Four animals in all were used.

The following results were obtained with ammonium carbonate:

Dog I, 7.2 kilos, received 5 gm. chloretone in 50 per cent. alcohol. Increase in weight of filter paper during the two control periods was 0.2 and 0.12 gm. The increase in weight after 0.3 gm. of ammonium carbonate for three periods of ten minutes each was 0.18, 0.14, 0.16 gm. respectively.

Dog II, 6.5 kilos, received 5 gm. chloretone in 50 per cent. alcohol. Increase in weight of filter paper during the two control periods

0.9 and 0.4 gm. respectively. The increase in weight after 0.25 gm. of ammonium carbonate for three ten-minute periods was 0.4, 0.4, and 0.4 gm. respectively.

Dog III, 7 kilos, received 5 gm. chloretone in 50 per cent. alcohol. Increase in weight of filter paper during the two control readings 0.19 and 0.17 gm. respectively. The increase in weight after 0.5 gm. of ammonium carbonate for three periods was 0.17, 0.16, and 0.17 gm. respectively.

Dog IV, 7.5 kilos, received 5 gm. of chloretone in 50 per cent. alcohol. Increase in weight of filter paper during the two control periods was 0.2 and 0.14 gm. respectively. The increase in weight after 0.25 gm. of ammonium carbonate for three ten-minute periods was 0.14, 0.12, and 0.12 gm. respectively.

These experiments show that at least by the method pursued ammonium carbonate in what would be called moderate laboratory doses for a dog does not increase bronchial secretion. The dosage varied from 0.25 to 0.5 gm., equivalent to 2 to 4 gm. for a 65 kilo man, an amount considerably in excess of the ordinary therapeutic dose.

Both experimental and clinical evidence would indicate that the iodides cause increased secretion of bronchial mucus. Henderson and Taylor, from their experimental report, believe that this must be due to reflex stimulation of the bronchial centre from the stomach, as in their experiments iodides used intravenously did not modify the bronchial secretion. The iodides, as shown by Baehr and Pick and others, also cause dilatation of the bronchioles. It is possible this may play some role in facilitating the removal of mucus.

Many of the drugs having an emetic action also act as expectorants. Attention has already been called to the apparent intimate relation between the salivary and bronchial gland centre. The most important members of this group are apomorphin and ipecac. Both of these in non-emetic doses are supposed to cause increased bronchial secretion. Apomorphin probably acts chiefly by direct stimulation of the bronchial gland centre; ipecac both centrally and reflexly from the stomach. These drugs when pushed to the point where they have an emetic action may possibly through their vagus action also cause increased peristalsis of the smaller bronchioles. Senega, according to Henderson and Taylor, probably acts as an expectorant by effecting the bronchial gland centre reflexly from the stomach. Pilocarpin stimulates the bronchial glands directly.

Rossbach, Calvert, and Henderson and Taylor agree that ipecac and apomorphin act as expectorants in animals. Calvert failed to obtain results with senega, but Henderson and Taylor produced marked increased bronchial secretion in cats. Henderson and Taylor also obtained positive results with antimony and tincture of squill. The uniformity of these results leaves no doubt that in

the doses used these drugs act as expectorants on dogs and cats. Henderson and Taylor call attention to one point, namely, that the bronchial gland centre is easily depressed and then fails to act. Especially with apomorphin a slight excess in dosage by depressing this centre would lessen bronchial secretion. They raise the question whether in diseased conditions with marked circulatory disturbance the bronchial gland centre would react as in the normal.

The dosage employed in all this experimental work was quite large. Henderson and Taylor gave 1 c.c. of the fluidextract of ipecac intravenously and 2 c.c. of the wine of ipecac by the mouth to a $2\frac{1}{4}$ kilo cat. This would be equivalent to 25 and 50 c.c. in man. This dose is, of course, far in excess of that employed clinically. Their results with senega and quill were obtained by using 2 c.c. of the tincture of each in a 2.5 kilo cat: here, again, doses far in excess of that employed in man. They have not, therefore, proved that any of these drugs are active in the ordinary therapeutic doses, which after all, from a clinical standpoint, is most important. For this reason we thought it desirable to repeat these experiments, using moderate doses.

The expectorant action of ipecac and apomorphin was tested on four dogs. The method of procedure differed very slightly from that used in the experiments with ammonium carbonate. After severing the trachea the roll of filter paper was introduced into the upper portion rather than the lower, as in the previous experiments. This method offers two advantages: (1) that absorption of moisture from the expired air is avoided; and (2) only mucus from the surface in contact with the filter paper is obtained, as in the previous method much mucus may be carried upward by ciliary action.

Chloretone was employed as an anesthetic in three of the animals, urethane in one. The emetin was injected directly into the stomach, the apomorphin into the duodenum. In each instance the filter paper was allowed to remain in contact with the mucosa ten minutes. Two control readings were taken before administering the drug. Readings were taken for at least forty minutes after giving the drug, which should be sufficient time to permit of a physiological action occurring.

The following results were obtained with emetin hydrochloride:

Dog V, 7.8 kilos, received 5 gm. of urethane and 2 gm. of chloretone in 20 c.c. of 50 per cent. alcohol. Increase in weight of filter paper during the two control periods 0.65 and 0.69 gm. respectively. The increase in weight after 4 mg. of emetin hydrochloride for three periods of ten minutes each was 0.262, 0.0525, and 0.0495 gm. respectively.

Dog VI, 6.7 kilos, received 5 gm. of chloretone in 20 c.c. of 50 per cent. alcohol. Increase in weight of filter paper during the two control periods was 0.0613 and 0.062 gm. respectively. The

increase in weight after 4 mg. of emetin hydrochloride, for three periods of ten minutes each, was 0.058, 0.056, and 0.05 gm. respectively.

The following results were obtained with apomorphin sulphate:

Dog VII, 9 kilos, received 2.5 gm. of chloretone in 15 c.c. of 50 per cent. alcohol. Increase in weight of filter paper during two control periods was 0.08 and 0.0746 gm. respectively. The increase in weight after 2 mg. of apomorphin for three periods of ten minutes each was 0.0727, 0.0664, and 0.0643 gm.

Dog IX, 8 kilos, received 5 gm. of chloretone in 20 c.c. of 50 per cent. alcohol. Increase in weight of filter paper during the two control periods was 0.06 and 0.055 gm. respectively. The increase in weight after 2 mg. of apomorphin sulphate was 0.054, 0.058, and 0.055 gm. respectively.

It will be noticed that the first reading in each instance was considerable higher than the subsequent ones. This can probably be accounted for by mucus which had collected in the trachea, and, therefore, does not represent the real secretion during the period. At the beginning of the experiment there was frequently slight bleeding from the severed end of the trachea; this added to the weight of the filtered paper.

The apparently much greater secretion of mucus in Dogs I to V in both controls and after receiving the drug was due to the roll of filter paper being introduced in the lower segment of the severed trachea, so that much of the mucus on the filter paper was carried up by the cilia from below and also from moisture in the expired air. The filter paper was introduced into the upper end of the trachea in Dogs VI to IX, the increase in weight here probably being due almost entirely to mucus secreted from the surface covered by the filter paper.

I wish to express my appreciation of the valuable suggestions and assistance rendered by Prof. A. P. Matthews, of the University of Chicago.

SUMMARY. Ammonium carbonate and ammonium chloride and the emetic group of expectorants, as apomorphin and ipecac, when given in sufficiently large doses to animals, increase bronchial secretion. Ammonia salts per os, in moderate doses equivalent to 2 mg. in an adult man, do not increase bronchial secretion in the dog. Apomorphin and emetin when given to dogs in doses considerably greater than the ordinary therapeutic dose for man do not excite increased bronchial secretion.

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RELATIVE PULMONIC INSUFFICIENCY.

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DENVER, COLORADO.

IN the study of the valvular diseases of the heart, a general agreement among clinicians may be noted in almost every field excepting the one we are to study.

Mackenzie, Dieulafoy, and many other writers do not even mention in their text-books the possibility of relative insufficiency at the pulmonary orifice. Jurgensen was evidently familiar with the murmur, but apparently failed to interpret it correctly. He states,¹ in describing the different types of murmur to be found in mitral stenosis, that "the diastolic murmur is also heard at times in the second left intercostal space, in the region of the pulmonary artery or a little outward from that point. At times the murmur is heard a little more distinctly in that locality than at the apex, especially when a systolic murmur is also present at the latter." It is certainly a most striking circumstance that he describes so closely the murmur we study in the very type of case in which it is most frequently noted. He makes no direct mention elsewhere of the lesion we are considering.

Among the authors at hand who mention the phenomenon definitely are Colbeck, who states that "relative incompetence of the pulmonic valve does sometimes occur, but the lesion is decidedly rare. It . . . may obtain in cases of mitral stenosis."

Satterthwaite states that "temporary insufficiency is doubtless of common occurrence."

Osler² says that "both Gibson and Graham Steell have called attention to the possibility of leakage through these valves in cases of great increase of pressure in the pulmonary artery, and to a soft diastolic murmur heard under these circumstances, which Steell calls "the murmur of high pressure in the pulmonary artery."

¹ Nothnagel's Encyclopedia, Diseases of the Heart.

² Eighth edition.

Allyn³ says that "it is probable that relative pulmonary insufficiency occurs more frequently than we are wont to believe."

Further quotation of authorities would simply emphasize the lack of unanimity of opinion as to the possibility and frequency of the condition.

Gibson's experiments should be quoted in order to show the reasonableness of the diagnosis of relative insufficiency under conditions of high pulmonary arterial pressure. "In the healthy human heart much fluid escaped (from the pulmonary orifice) with a pressure above thirteen inches, a small amount between thirteen and eight inches, and none below that pressure. We have no direct means of estimating the pressure in man. The results of animal experiments give as the mean pressure, 17.6 mm. of mercury in the cat, 12.07 mm. in the rabbit, and 29.6 mm. in the dog (Bentner). Eight inches of water is equal to about 15 mm. of mercury, so that the pressure in the pulmonary artery in man at the height of a vigorous systole of the right ventricle may cause a pressure well above that which first begins to cause insufficiency."⁴

Analogy would lead us to expect to find relative leakage here as at other valves, and it is therefore difficult to understand the position of certain authors who ignore the existence of the condition, or virtually state that it does not occur.

Personally, I regard relative pulmonary regurgitation as being a not very infrequent complication of advanced mitral stenosis and extensive fibroid phthisis, and as being occasionally found in other conditions in which the pulmonic tension is high.

In "A Clinical Study of Six Hundred Cases of Heart Disease"⁵ I found the murmur in question present three times in association with mitral stenosis: once in association with double mitral disease, and once in association with combined aortic and mitral regurgitation. The total number of cases of simple mitral stenosis studied in this series was 35, while 44 cases presented double mitral murmurs. We may safely assume, I believe, that if the signs and symptoms to be mentioned warrant the diagnosis of relative pulmonary insufficiency the affection may probably be found in possibly from 3 per cent. to 5 per cent. of cases of mitral stenosis. My experience before and since the gathering of the statistics quoted (between 1903 and 1909) confirms me in this opinion.

The diagnosis rests upon the association of the following findings:

1. Some definite cause for increased pulmonary tension, notably mitral stenosis or fibroid phthisis in an advanced state.
2. The presence of increased precordial area of dulness, especially suggesting dilatation of the right ventricle.
3. The presence of a soft diastolic murmur heard at the region of the pulmonary valves, and transmitted downward from the

³ AMER. JOUR. MED. SCI., October, 1913, No. 4, cxlvii, 51.

⁴ Quoted from Osler's System of Medicine.

⁵ Med. Record, November, 13, 1909.

second or third left intercostal space along the left side of the sternum. The murmur is exactly of the type found in aortic regurgitation, excepting that it is generally more soft and blowing in character. The most striking single feature is the inconstancy of the murmur. After being present for days or weeks, with the regaining of a better condition of compensation, the murmur disappears, to reappear with the next breakdown. It is absolutely essential to the diagnosis that the aortic valve sounds be clear and that no feature of aortic regurgitation be present. Fortunately, the insufficient filling of the left ventricle in mitral stenosis often-times renders the aortic second sound so notably feeble that the pulmonary signs are prominent by contrast.

4. Absence of thrill. This is not infrequent in the organic lesion, but is, I believe, never found in relative insufficiency, and should therefore count against such a diagnosis. The presence of a systolic murmur at this orifice would militate against the diagnosis of relative leakage and be in favor of the organic type.

5. The murmur may be increased in intensity by expiration, especially with the closed glottis, the increased intrapulmonary pressure being the active agency in bringing about the exaggeration of the murmur. A similar increase may be noted after exertion.

As is to be expected, the pulmonary second sound is commonly enfeebled by the failure of close apposition of the pulmonic leaflets.

Of the considerable number of cases which I have seen I shall quote but two.

CASE I.—Male, aged twenty-seven years, complained of dyspnea and cough, the former of extreme severity. Cyanosis was present at various times while under observation. Edema finally appeared. The heart was much increased in area, the apex-beat being found 12 cm. to the left of the central line, with marked presystolic murmur and thrill. A soft diastolic murmur was found extending downward from the third left interspace. This disappeared under rest in bed and the administration of digitalis. There were none of the features of aortic regurgitation.

The patient later passed through an attack of acute pneumonia, the murmur reappearing. Recovery ensued, this being one of the few cases I have known of recovery from acute pneumonia in advanced mitral stenosis. Within a year the patient died of cardiac incompenstation. The postmortem examination showed a marked "buttonhole" mitral valve, with hypertrophy and extreme dilatation of the heart. The aortic, tricuspid, and pulmonic valves were normal.

This case was shown at a meeting of the Denver County Medical Society, and the presence of a murmur of the character described was verified by many of those present.

CASE II.—A female, aged thirty-three years, had suffered twice from acute rheumatism. She presented at the single examination which I had the opportunity of making, enormous dilatation of

the heart, the transverse diameter of the precordial flatness being 20 cm. The great increase in this direction is well shown in the accompanying skiagram, for which I am indebted to Dr. G. H. Stover. A loud presystolic murmur was present at the apex, with presystolic thrill. At the pulmonic area there was heard a diastolic murmur such as we have described, transmitted downward, and increased in intensity by exertion.

The aortic second sound was notably feeble, and no signs of aortic insufficiency existed. In the skiagram may be noted at *a* the marked dilatation of the right ventricle, and the general increase in area in a transverse direction as mentioned above (60 per cent according to Dr. Stover's measurements). In the absence of post-mortem proof in this case we can, of course, make only a presumptive diagnosis of relative insufficiency.



Skiagram of Case II, showing increased transverse diameter of the dilated heart.

In view of the evidence of mitral obstruction, of the pulmonic diastolic murmur, increased in intensity upon exertion, absence of thrill, absence of signs of aortic disease, feeble aortic second sound, the known rarity of organic pulmonary regurgitation and the entire reasonableness of a diagnosis of relative leakage at the valve mentioned under conditions of marked increase in the tension of the pulmonary circulation, the diagnosis in this and similar cases, in my opinion, rests upon as secure a basis as that of the other valvular diseases of the heart.

THE PREVENTION AND TREATMENT OF VULVOVAGINITIS IN CHILDREN.¹

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THE 66 cases of vulvovaginitis upon which this report is based occurred sporadically during the past eighteen months in girls varying in age from three weeks to twelve years, most of whom were referred from the St. Louis Children's Hospital Dispensary to the Washington University Gynecological Dispensary for treatment. Forty-three of these patients were investigated as to home conditions, possible source of infection, etc., by the social service department of the Children's Hospital. My thanks are due to Miss Stimson, the head of the department, and to Mrs. Marshall, who investigated most of the cases, for their kind coöperation and assistance. I also wish to thank Dr. Stewart, of the department of hygiene of the Board of Education, and the Visiting Nurses' Association for the assistance given me in the treatment of a large number of these cases.

The importance of gonorrheal vulvovaginitis in children lies not merely in the physical discomfort and occasional serious complications resulting therefrom, but in the moral shock produced upon the child and the family by the occurrence of this loathsome disease in the midst of the innocence of infancy and childhood. Possibly because it occupies a sort of midway position between pediatrics and gynecology, few specialists have given this disease the serious consideration it merits. The epidemics of vulvovaginitis that have from time to time invaded children's hospitals and institutions have aroused pediatricians to the contagiousness of this infection. The profession at large has not, however, seemed to realize that a condition so infectious in institutions must also be frequently transmitted from child to child, or through some other agency, outside of such hospitals or institutions. Particularly in schools, in tenements, in public playgrounds, etc., wherever children congregate in considerable number, and the same lavatories, towels, etc., may be used, we have conditions favoring infection. That the disease is far more common than was formerly supposed is being generally recognized. Seippel² estimates the number of cases occurring annually in Chicago at 500. Pollock³ believes that from 800 to 1000 girls are yearly infected in the city of Baltimore. The number of cases in this report coming from practically one

¹ Read before the St. Louis Medical Society, May 9, 1914.

² Cited by E. R. Spankding, *Amer. Jour. Dis. Children*, 1913, v, 266.

³ The Acquired Venereal Infection in Children, *Bull. Johns Hopkins Hosp.*, May, 1909, xv, 142.

source in eighteen months is evidence of the prevalence of this disease in St. Louis. Furthermore, Dr. Jeans, the resident pediatrician of the Children's Hospital, undertook over a period of five months a routine examination of all children coming to the Children's Hospital Dispensary to determine how frequently this condition passed unrecognized; 262 girls over one year old were examined, and whenever any moisture or secretion was seen it was examined for gonococci; 14 children were found to be infected, that is to say, about 5.3 per cent. of all girls coming to the dispensary. Only a small number of the 14 children in whom the infection was found came on account of the discharge.

ETIOLOGY. While in three of the cases that came under my observation the absence of gonococci and the character of the vaginal discharge and the rapidity with which it cleared up indicated some infectious or irritative condition outside of gonorrhea the remaining cases all showed at one time or another gonococci in the secretions. For practical purposes, therefore, vulvovaginitis should be termed gonorrhea. A correct appreciation of the etiological factors can only be obtained by considering the anatomy and histology of the lower genital tract in girls before puberty. Why is it that we find these infections not transmitted to little boys or to girls beyond puberty or to adults? The gonococcus grows most rapidly upon delicate squamous or cylindrical epithelium. Such delicate epithelium is found about the vulva and vagina in little girls, whereas in adults the epithelium is much denser and more resistant. Unfortunately the external genitals of girls are, so to speak, bare and everted before puberty, offering the best possible nidus for infection. With the increase in size of the labia majora, and above all the development of a hairy covering at puberty, the vestibulum vaginae is shielded from direct contact with the outside. In none of the cases that came to our clinic where we could exclude the possibility of sexual contact was there found any girl who was beyond puberty. This corresponds to the reports of other investigators.⁴

In analyzing the possible causes of this infection we must consider first the source, and secondly the manner of transmission. I realize of course the great difficulty of trying to analyze the various factors that deserve consideration, and feel that while we may have presumptive evidence along certain lines it is almost impossible, except in a few cases, to get absolute proof. The first question is whether the parents are the source of infection? Investigation showed that a large majority of these parents had had two or more children, that the mothers in only a few cases gave a history of a discharge, and that where a vaginal examination was made it was usually negative. In two instances, however, the mothers showed

⁴ Spaulding, loc. cit.; W. Hamilton, *Gonococcus Vulvovaginitis in Children*, Jour. Amer. Med. Assoc., April 9, 1910, i, 1196.

an acute gonorrhea preceding the infection in the child, and here she was probably the infecting agent. Other possible sources of infection are older brothers and sisters, other persons living in the same house or using the same lavatory, and finally other already infected girls of the same age. The last-named focus of infection is, as I will later try to show, the most important factor in the spread of the disease.

Now as to the manner of transmission. In only four children did the question of rape come up for consideration. In no case was there any external injury indicating this as likely. In one instance the mother accused a boy of sixteen as being responsible for the infection. He was arrested and an examination showed that he had not the slightest evidences of gonorrhea. German writers lay some stress upon the superstition among the lower classes abroad that an adult infected with gonorrhea can be cured by transmitting it to some innocent child. In none of my cases did this seem a probable explanation, and I was particularly impressed by the fact that only a few girls came from the ignorant, foreign-born population.

Etiological studies of the epidemics in children's hospitals indicate that the hand of the nurse may at times be a factor in the transmission of the infection. In how far can we consider this as of importance in the cases appearing sporadically in homes? Is the hand of the infected mother an important factor in transmitting infection to her child? I believe not. The small percentage of mothers who had a gonorrheal infection has already been noted. Even stronger evidence against this manner of infection lies in the fact that only two of our cases occurred in children under one year of age. Now just at this time the epithelium is most delicate and susceptible to infection, and the mother a dozen times a day is compelled to handle the genitals of the child. The relative absence of infection during these first twelve months speaks strongly, therefore, against the frequency of this manner of transmission.

Next we must consider the transmission through cloths, either in the form of clothing, towel, wash cloth, or bedlinen. The gonococcus, as is well known, is particularly susceptible to drying. While I am far from denying that this manner of transmission, especially through bedlinen, occurs from time to time, we must realize that cloth will absorb considerable of the secretion, and in the course of ten to fifteen minutes will ordinarily be dry enough not to be a serious source of infection.

We have yet to consider the bath and the lavatory as a means of transmitting infection. In institutions where a number of children are bathed one after the other it is readily possible that infection may be carried from one to another. We are, however, primarily concerned in this paper with the home cases, and here the greater interval between baths make the spread of gonorrheal

infection through this agency unlikely. In this country public baths are few in number, and usually consist of showers or a swimming-pool, where contamination of this sort would be uncommon.

In the lavatory seat, however, we have factors favorable for spreading this contagion. Secretion containing gonococci deposited here will, owing to the moisture of the surrounding air, remain a long time undried and virulent. Moreover, lavatories, even in grammar schools, are, as a rule, so high that the smaller children in using them are forced to have their genitals and clothing rub over a considerable portion of the seat. The greater the number of persons using the same lavatory the less interval of time is apt to elapse between its use, and hence the greater likelihood of carrying infection. The lavatory seat of the tenement-house districts is hence a source of great danger for little girls, particularly where it is rough or unclean. In the public schools, where at recess there is practically no interval in the use of the lavatory, the danger is even greater. Of course if we could keep all the infected girls from attending school the danger would be eliminated. We found, however, that a number of girls did not seek medical advice until after a profuse discharge had been present for several weeks, and that a number of lighter infections passed unrecognized and untreated for months. With the open formation of the genitals in girls and the unnatural high seat of the lavatory it is impossible for an infected child to avoid contaminating the seat with some of her discharge. I have not given figures regarding etiology from the social service investigation of the cases, because the evidence on which they were based varied so much in reliability. In some instances it was merely the statement of the mother. Where, however, we have record that a child of five years, whose parents, brothers, and sisters were free of gonorrhea, whose home lavatory was immaculate and used only by the family, became infected one and a half months after attending school, the interpretation can hardly be questioned. Furthermore, it is rather striking that in my own tabulation, as given below, 47 out of 66 girls were of school age or over.

Less than one year, 2; one to three years, 13; four to six years, 23; seven to nine years, 19; ten to twelve years, 9; total 66 cases.

I think, therefore, that it can be fairly said that the most frequent source of infection is from child to child, and that the most common manner of its transmission is through the school lavatory. This is in no wise a reflection upon the cleanliness of the public schools, but merely the result of special factors predisposing to contagion.

HOME CONDITIONS. While no portion of the city was exempt from this infection, not even the fashionable parts of town, the social service investigation revealed the fact that a majority of the families were of the poorer classes and lived in cramped quarters. Of the homes examined fifteen were extremely neat and clean,

ten were unsanitary in some respects, and nine of them were filthy. Only 11 of the 66 were colored girls. In the poorer homes and tenements there was usually one lavatory for the whole building used by everyone, and at times in bad condition. It was also common to find that the infected child slept with the mother or with a brother or sister. Until the social service worker or the visiting nurse visited the home there was usually not the slightest attempt at limiting the infection, and in three instances the result was that a sister of the patient had become infected.

SYMPTOMS. Few of the girls had pronounced discomfort. In the acute stage there was some increased frequency and burning on urination and a vaginal discharge. Usually, however, it was the mother who first noticed a yellowish stain upon her child's clothing, and on inquiry discovered the disease. Some children had a temporary enuresis during the active stage. At times the child would complain of feeling chafed. The course of the disease was almost invariably prolonged. Complications occurred rarely. Twice there was a gonorrheal proctitis, resulting from the use of an infant syringe for constipation. One patient had an attack of severe abdominal pain with fever and tenderness lasting one week, which in all likelihood was due to a tubal involvement. Two girls developed an ophthalmia, and one of these two likewise had an arthritis.

TREATMENT. So unsuccessful have been most of the methods of treatment suggested that some believe as much can be accomplished by simply leaving the cases alone. While realizing all the difficulties, I feel that such pessimism is not justified. Doubtless the general condition of the patient is an important factor. Fresh air, good food, and an iron tonic aid materially in effecting a cure. One child that had been under our care for almost a year, with but little relief, was cured by a summer in the country. In the acute infections, rest in bed, preferably in a hospital, supplemented by instillations of 25 per cent. argyrol give the best results. This should be supplemented by hexamethylamine, gr. i to iv, t.i.d. As to vaccine I agree with Dr. G. G. Smith,⁵ who recently stated: "We have not used vaccines, nor do we believe their employment in gonococcic infection of the mucous membranes, whether in the male or in the female, has up to the present given sufficiently satisfactory results to warrant any dependence on them."

An extended trial was made of the effect of the lactic acid bacillus. The tablets made by Parke, Davis & Co., were crushed and about 5 grains of the powder made into a small vaginal cocoa-butter suppository. The insertion of these suppositories was at times attended with some difficulty. These treatments were given three times a week for six to eight weeks. In three out of the ten cases in which this treatment was used there was a temporary

⁵ Treatment of Gonococcic Vulvovaginitis, Amer. Jour. Dis. Children, March, 1914.

cessation of discharge. In the other cases the result was so questionable that this form of treatment was abandoned.

I abstained from using the dry powder treatment with bolus alba⁶ and xerase,⁷ partly because of the numerous failures in the hands of others, but mainly because it is anatomically impossible of application. I had the same anatomical objections to the use of the vaginal douche in children. The corrugated surface of the vagina in these patients offers little if any opportunity for the effective use of either powders or irrigations. Moreover, we have but rarely sufficient discharge in the vagina to justify a douche. A more rational method to my mind is the repeated instillation, under slight pressure, of a small quantity of a somewhat stronger antiseptic solution. For this purpose I used the ordinary small rubber-tipped urethral syringe, pressed tightly over the hymeneal orifice. In accordance with the age of the child, from 15 to 60 drops of the solution are injected several times in succession. This balloons out the folds of the vagina and allows the solution to come in contact with every portion. While I favor the less irritating silver preparations in the very early stages, I found it best to go over as soon as possible to a 1 per cent. silver nitrate solution. In the last twenty-one cases treated over a period of five months I have been using 2 per cent. and even 4 per cent. silver nitrate solutions. It is surprising how little burning these stronger preparations caused and how satisfactory were the results obtained in the chronic cases. The 2 per cent. silver nitrate solution was used in girls under five years of age, and in those over five years the 4 per cent. solution was used once or twice a week in the late stages with good effect. I find no record of the use of such strong solutions by others, and believe my favorable results and the absence of any untoward symptoms justifies a further test of this treatment. My outline of treatment for vaginitis in a girl of school age would therefore be: first two weeks, rest in bed as much as possible, 25 per cent. argyrol injected twice daily if in hospital; third to fourth week, daily instillations of 1 per cent. silver nitrate solution; fifth to sixth week, instillations of 2 per cent. silver nitrate solution every other day; seventh to tenth week, instillations of 4 per cent. silver nitrate solution twice and later once a week. Finally if there is no more discharge for over a month, send to the country for one to two months without treatment.

Any form of treatment, however, will fail if it is not carried out systematically over a long period of time. Mattisohn⁸ complains that his results were frequently spoiled because parents failed to bring their children regularly. To overcome this I secured last

⁶ Nassauer, rev. in *Zeitsch. f. Kinderheilkunde*, 1913, iv, 111.

⁷ Cronbach and Tojbin, rev. in *Zeitsch. f. Kinderheilkunde*, ii, 224.

⁸ Die Prognose der Vulvovaginitis Gonorrhoeica Infantum, *Archiv f. Dermatol. u. Syph.*, cxvi, 817-840.

November the assistance of the Visiting Nurses' Association. On Saturdays the children were seen at the dispensary, treatment given, and the nurse who was present instructed in the home treatment for the coming week. Every day or every other day, depending on the case, the nurse gave the treatment at home and reported anything unusual to me. During the previous year, when we had no such system, we found that the mother soon tired of bringing her child until a bad relapse again forced her to have something done. Such haphazard treatment is hardly better than none at all.

PROGNOSIS. The results of treatment are difficult to judge because of the impossibility of saying whether a case is cured or not. The results of Dr. Smith's⁹ complement-fixation tests, particularly his second report published in March, 1914, indicate that even with this test we are at a loss to say positively when a cure is effected. This is, however, very different from denying the possibility of cure. Mattisohn⁸ has shown that even without active treatment eighteen out of thirty-one girls, after a period of two to five years, showed no discharge or gonococci, and that with active treatment about 75 per cent. should be cured in three to four months. Insufficient time has elapsed to state the outcome of a majority of our own apparent cures.

About 150 slides of vaginal secretion were examined microscopically in the course of the weekly treatments of the 19 cases that came to the dispensary since November 29. These slides were taken from every case once a week and brought out a number of interesting points: the frequency of recurrences or slight exacerbations, the change from a purulent to an epithelial discharge, the variation in bacterial flora, etc. I was repeatedly surprised how in the presence of but little discharge numerous intracellular gonococci were found. One typical record will serve to illustrate the course of the infection:

Dora W., aged three years. Smears showed:

November 29. Considerable pus, some intracellular and extracellular gonococci. No other bacteria. A few epithelial cells.

December 6. Considerable pus. Still a few intracellular gonococci.

December 13. A few leukocytes. Much epithelium. No gonococci.

December 20. Some pus. Considerable epithelium. Many bacteria, a few extracellular gonococci (?).

December 27. A few leukocytes. Epithelia abundant. A few extracellular diplococci.

January 3. Increased pus, some epithelium. A few intracellular gonococci.

⁹ Complement-fixation Test in Gonorrheal Vulvovaginitis, Amer. Jour. Dis. Children, 1913, v, 313-316.

January 10. Epithelium abundant; no pus; many bacteria.

January 17. Epithelium abundant; few bacteria.

January 24. Only epithelium.

February 14. A few epithelia; no pus; no bacteria.

February 28. Nothing on slide.

April 11. Only epithelia.

Some say these exacerbations of gonorrhea are due to reinfection, but this seems very unlikely. Usually the microscope has still shown some leukocytes present, even though there was no visible discharge. The isolation employed would exclude the possibility in most of our cases of reinfection as a cause. That there is a chronic nongonorrheal vaginitis following upon the wake of the true infection, as claimed by Smith,⁴ characterized by a chalky discharge, consisting almost wholly of epithelial cells, my examinations would corroborate. I do not think all these cases should be classed as uncured.

The ultimate danger to the child through this infection is difficult to estimate, although it probably rarely amounts to much. Yet every now and then we come across a case like the following:

Miss W., aged twenty-five years, consulted me May 11, 1914. She had had, ever since five years of age, some frequency of urination and a vaginal discharge. Was treated for pinworms by her family doctor. Dysmenorrhea since sixteen years of age. Pelvic symptoms. Examination shows hymen intact, urethra reddened, some mucopurulent vaginal discharge. Uterus retroverted. Tubes thickened, adherent, tender. Diagnosis: salpingitis and retroversion following gonorrheal vaginitis.

PREVENTION. I have left the consideration of preventive measures to the last because of its importance. Holt,¹⁰ Spaulding,¹¹ and others have suggested measures for the prevention of epidemics in children's hospitals, orphans' homes, and similar institutions. These consist of the following:

1. The examination of a vaginal smear from all girls before admission to determine the presence of gonorrheal infection. If present, the children are excluded.

2. Adequate facilities for isolating institutional cases with this infection in whom the diagnosis had not been made on admission.

3. Special nurse, separate fever thermometers, vaselin, etc., for the infected children.

While strict adherence to these precautions will almost invariably prevent epidemics in institutions, it does not influence the large number of endemic cases constantly to be found in our large cities. Very little thought and energy has thus far been directed to control

¹⁰ Gonococcic Infection in Children, New York Med. Jour., March 18, 1905, lxxxi, 521.

¹¹ Alice Hamilton, Gonorrheal Vulvovaginitis in Children, Jour. Infect. Dis., March 30, 1908, v, 147.

the spread of infection along these channels. Recently the Health Commissioner of New York, Dr. Goldwater, received a communication from the Superintendent of the City Schools of New York, stating that forty-eight children in the schools had been inoculated with some "loathsome disease" in the public hospitals of the city. Investigation showed that the municipal hospitals were not to blame, but that the disease was sufficiently prevalent to justify the serious consideration by the Health Department. I quote the following from his report.¹²

"That a form of vaginitis, which is bacteriologically indistinguishable from gonorrheal vaginitis, is a common condition among children in this city and elsewhere, is well known to clinicians.

"If a serious attempt were made to exclude from school all children who suffer from vaginitis, it would be necessary (a) to establish the machinery by which a complete physical examination of all female school children could be made; (b) to convince the public of the necessity of the proposed measure; (c) to establish the legal and moral right of the city authorities to require such an examination. Furthermore, inasmuch as the condition in question is one which, notwithstanding the most intensive treatment, often persists for months and even for years, it would be necessary to inaugurate a method whereby the education of excluded children could be continued. The only logical method would be to send private teachers into the homes of infected children.

"The questions here involved are among the most difficult and puzzling with which public health administrators have to deal. I am not aware that the problem has been solved anywhere, and can only promise, on behalf of this department, unremitting attention to it, in the hope that a working program may ultimately be formulated."

The interest of a man of Dr. Goldwater's experience in this problem will help greatly in its effective solution.

I should like to suggest the following additional preventive measures for the control of this disease:

1. *The instillation of a drop of 2 per cent. silver nitrate solution in the vestibulum vagina of all newborn girls whose mothers show evidence of gonorrhea.* I realize of course that probably not over 5 per cent. of the cases of vaginitis are infected at birth, but it seems to me that, particularly in maternity institutions, this precaution could certainly do no harm and would prevent a number of infections.

2. *Making vaginitis in children a disease reportable to the Board of Health.* It is probable that this would meet with considerable opposition at first, but since the disease is acquired innocently and usually from sources outside of the family, there could be no

¹² Cited in *The Modern Hospital*, May, 1914, p. 305.

question of violating professional secrecy by making such a report. If the Board of Health does not feel authorized to ask for such reports children attending the public schools could at any rate be reported to the department of hygiene of the schools so that the necessary steps to exclude their attendance during the active stage of the disease could be arranged for. Such reports to school authorities have been made by us for the last six months. I realize of course that there must be an element of compromise in this situation. We would not be justified in excluding the children from school for eight or nine months because of this disease unless there existed a special school, like the Frances Juvenile Home, in Chicago, where children with this disease could be given the necessary instruction. In St. Louis I have adopted the plan of allowing the children to return to their school work after about two months' treatment, provided there has been no visible discharge for several weeks. The teacher is, however, notified by the visiting nurse that the child is not to use the school lavatory. The nurse also sees to it that the child reports to the dispensary, at first once a week, later twice a month for reinspection over a period of five months. In case of any recurrence the child is kept out of school again until the active stage has completely subsided.

3. *Instruction of parents of infected children through the visiting nurse regarding preventive measures to limit the infection.* These measures would include the use of separate towels and wash-cloths, sleeping in a separate bed, care as to a thorough cleansing of any contaminated clothing, and special precautions in the use of the lavatory. It would of course be best for the child to use its own vessel instead of the common lavatory.

4. *Investigation by the visiting nurse as to the probable origin of the infection in each case with a view to excluding this factor from contaminating other children in the same house.* This would include the inspection of tenement lavatories, with a report to health authorities if they were found in an unclean condition. It would also include the supervision of infected children not attending school, or not of school age, to see that proper treatment is employed.

5. *The adoption of a U-shaped seat with low bowl and other precautionary measures to prevent the spread of infection through the public lavatories in schools, playgrounds, comfort stations, and tenements.* I consider this last-named suggestion the most important of all, and there is no valid reason why it could not to a large measure be put into operation at once. Paper coverings for lavatory seats have been used for purposes of cleanliness in some of the large hotels, and their employment in public places, such as schools, playgrounds, etc., would probably diminish the chance for infection. As, however, children could not be relied upon to apply such papers properly, it would be safer to use the U-shaped seat in addition. The height of the bowl should not be over eight inches where the

lavatory is to be used by children of school age. The presence of an attendant in the school lavatories, especially during recess, would aid materially in the discovery of girls having a discharge, in the proper use of the paper covers, and in the general cleanliness of the lavatory.

Gonorrhea in adults is so intimately connected with the public morals that any marked diminution in its prevalence seems like trying to reform the universe. Gonorrhea in little girls, on the other hand, is simply the result of inadequate sanitary precautions. The fact that hundreds of little girls are innocently infected with it every year in our large cities is a disgrace to the hygienic methods of the beginning of the twentieth century. Certainly we can say of gonorrheal vaginitis in children that one ounce of prevention is worth many pounds of cure.

DIRECT EXAMINATION OF THE DUODENAL CONTENTS (ALSO BILE) AS AN AID IN THE DIAGNOSIS OF GALL-BLADDER AND PANCREATIC AFFECTIONS.¹

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THE diagnosis of gall-bladder lesions is based upon the physical findings of the upper right abdomen in conjunction with the subjective symptoms and the objective data obtained. In typical cases of gall-stone disease there is no difficulty in recognizing the affection.

The characteristic symptoms are as follows: severe attacks of sudden pain in the upper abdomen appear at comparatively long intervals or years; they radiate to the back, often to the right shoulder-blade; are intense; last a few hours, or at the utmost two to three days, and leave as suddenly as they come. Frequently hypodermic injections of morphin have to be resorted to. During the attack the liver is usually increased in size; sometimes a more or less icteric discoloration of the eyes or skin is encountered; at times pronounced jaundice exists. A slight rise of temperature is often present in some of the attacks. During the interval there is perfect euphoria.

Frequently, however, the typical picture is lacking, and here we are at a loss to determine the trouble.

Still greater difficulties are encountered in the diagnosis of pancreatic lesions. A study of the function of this important organ

¹ Read before the American Gastro-enterological Association, at Atlantic City, N. J., June 22, 1914.

has been frequently undertaken in an indirect way either by examining the feces for the trypsin ferment or the gastric contents with its returned duodenal juices after the ingestion of olive oil into the stomach (Boldyreff's method). In neither of these methods the pancreatic juice can be obtained in a pure state, and therefore cannot be studied in a comprehensive manner.

During the last four to five years I have frequently attempted to obtain the duodenal contents in a direct way in appropriate cases. Some of the results were published in 1910.² In the present article I shall describe some of my new experiences relating to gall-bladder and pancreatic affections. We intentionally selected merely those cases in whom the diagnosis had been confirmed by operation or in whom the further course of the disease corroborated the clinical diagnosis. For convenience we give a summary of these cases in table form:

In looking over the table the following items are worthy of consideration: Two cases of catarrhal jaundice showed the presence of mucus in the duodenal contents; the bile appeared scantily, was clear, and revealed an admixture of mucus at intervals. In 15 cases of cholecystitis with gall-stones the bile was turbid in 13; in 2, however, it was clear. In 5 cases with turbid bile the gall-stones were found at the operation. Of the 2 cases with clear bile in 1 two small stones were passed a few days later and discovered in the stool. In one case with echinococcus of the liver the bile was dark green, turbid, with some blood admixed.

Among 6 cases with pancreatic lesions the pancreatic secretion in 4 of the cases showed absence of one or two ferments, while in two with pancreatic tumors, verified by operation, the pancreatic secretion a few days prior to the operation revealed the presence of all three enzymes. Sugar was found in the urine in 2 of these cases.

In trying to utilize the experiences gained from the above table the following deductions appear justified:

1. The macroscopic appearance of the bile is of great diagnostic import. If it is golden yellow and clear it usually indicates a normal gall-bladder. When the fresh bile looks greenish yellow and is somewhat turbid it portends a diseased state of the gall-bladder, which frequently contains gall-stones. Golden-yellow bile containing mucus is frequently observed in catarrhal jaundice. A pure golden-yellow bile may, however, occasionally exist notwithstanding the presence of gall-stones (Case M.).

2. Duodenal contents containing bile and pancreatic secretions permit gauging the pancreatic function.

3. The presence of the three ferments in sufficient quantity speaks for a normal activity. If one of the ferments is constantly absent

² Max Einhorn, Experiences with the duodenal Contents, Jour. Amer. Med. Assoc., July 2, 1910.

CASES OF GALL-BLADDER AND PANCREATIC AFFECTIONS IN WHOM THE DUODENAL CONTENTS WERE DIRECTLY EXAMINED (1911 TO MAY, 1914).

No.	Name.	Diagnosis.	Stomach contents.	Examination of duodenal contents.				Appearance of duodenal contents.	Microscopic examination of duodenal contents.	Remarks.
				Date.	Amylopsin mm.	Steapsin mm.	Trypsinogen mm.			
1	M.	Icterus, catarrhal.		April 13, 1912	+	0	2	Yellow, mixed with mucus.		
2	K.	Icterus, catarrhal.	HCl + Ac. = 46	" 20, 1912	+	10	0	Yellow, turbid; bile appears only some time after respiration; occasional blood specks; mucus.	Red-blood cells; mucus, blood pigment; crystals, bacillus pyocyaneus; bacillus coli communis.	
				" 28, 1912	2	4	3			
				Feb. 14, 1914	2	8	8			
3	T.	Cholelithiasis; virus tholent.	HCl + Ac. = 70	Feb. 25, 1913	4	0	0	Greenish-yellow, alkaline.		
4	L.	Cholelithiasis; virus ventriculi; appendicitis.	HCl + Ac. = 80	April 4, 1913	3	1	3			
				April 20, 1913	3	5	1.5			
5	F.	Cholecystitis; atonia ventriculi.	HCl + Ac. = 30	Jan. 22, 1912	0	0	2	Yellow, turbid; alkaline.		
				" 23, 1912	10	0	2			
				Feb. 2, 1912	Trace.	+	30			
6	E.	Cholecystitis; icterus.	" 17, 1912	3	0	0	Yellowish-green, turbid; yellow.	Mycelia.	Operated.
				" 21, 1912	12	+	+			
				Mar. 12, 1912	+	0	3			
7	Mrs. F.	Cholecystitis; cholelithiasis	HCl + Ac. = 76	Feb. 10, 1912	+	+	+	Somewhat turbid		
8	D.	Cholecystitis; cholelithiasis; atonia ventriculi.	HCl + Ac. = 60	Dec. 6, 1912	2	1	0			
				" 8, 1912	4	5	2			
9	Mrs. E.	Cholecystitis.	HCl + Ac. = 76	" 17, 1912	3	2	2	Turbid, mucus; alkaline = 20; sp. gr. = 1.008	Leucin; cholesterol crystals.	
				April 11, 1913	4	4	2			
10	Mrs. P.	Enteroptosis; cholecystitis.	HCl 0 Ac. = 26	Sept. 6, 1912	12	0	2	Thick, turbid, dark yellow-green; yellow, turbid.	Bacilli.	
				April 4, 1914	5	3	4			
				" 7, 1914	6	1	1			

11	Mrs. R.	Cholecystitis.	HCl + Ac. = 60	Jan. 17, 1914	+	2	0.5	Yellowish green, turbid; alkaline.		
12	Miss G.	Dilatation ventriculi; cholelithiasis; cholecystitis.	HCl + Ac. = 70	Mar. 30, 1914 " 31, 1914	20 12	1.5 15	3 10	Whitish gray, turbid; golden yellow, turbid.		
13	Miss S.	Cholelithiasis; ulcerus duodeni	HCl + Ac. = 80	April 3, 1914 " 4, 1914	11 15	2 10	15 20	Turbid, greenish; turbid, yellow-green; blood present.	Boas-Oppler bacilli.	Operated.
14	Mrs. M.	Ulcerus ventriculi; inflammation; cholelithiasis.	April 12, 1913	10	2	3	Golden yellow, clear; alkaline.		
15	Mrs. P.	Echinococcus of liver.	Mar. 11, 1913	8	Trace.	5	Dark green, turbid; neutral; blood present.	Red-blood cells; bacteria.	Operated.
16	Mrs. W.	Cholecystitis; enlargement of liver.	HCl 0 Ac. = 25	Nov. 29, 1911	Present.	0	Present.	Dark green, alkalinity equals 25.		
17	J. B. D.	Cholelithiasis.	HCl + Ac. = 65	Mar. 15, 1911	Present.	Present.	Present.	Yellow, turbid; alkaline.	Operated.
18	Mrs. B.	Cholelithiasis; icterus.	HCl +	Feb. 17, 1914	Turbid, bloody; no bile; alkaline	Operated.
19	Mrs. J.	Cholecystitis; pancreatitis; chronic.	HCl 0 Ac. = 20	Oct. 10, 1912	Present.	Trace.	Absent.	Alkaline.	Operated.
20	Dr. S.	Achylia gastrica; cholelithiasis; icterus; pancreatitis.	HCl 0 Reaction faintly acid.	Mar. 30, 1913	6	0.5	0	Faintly yellow; alkaline, turbid.	Streptococci.	Operated.
21	M. S.	Tumor of liver; pancreatitis; chronic or neoplasm; icterus.	HCl + Ac. = 40	Feb. 13, 1914	4	2	1	Turbid, white; no bile; alkaline.	Long chain, non-hemolytic streptococcus; bacillus coli communis.	Operated; urine contained bile and 2 per cent. sugar.
22	M. P. D.	Ulcer of stomach; cirrhosis of liver; pancreatitis.	HCl + Ac. = 48	Jan. 13, 1913	0	12	2	Yellow, somewhat turbid.	Urine contained 1 per cent. sugar.
23	Mrs. S.	Achylia gastrica; pancreatitis; chronic.	HCl 0 Ac. = 1	Nov. 9, 1913	2	2	0	Golden yellow; bloody.		
24	W. Z.	Pancreatic tumor.	HCl + Ac. = 80	Mar. 12, 1913	Present.	Present.	Present.	Yellow, slightly turbid.	Operated.

it usually indicates chronic pancreatitis. A tumor of the pancreas may, however, exist notwithstanding the presence of all the three ferments (Cases M. S. and W. Z.). This apparently surprising fact finds its explanation in the circumstance that the tumor has yet left enough healthy tissue in the rest of the pancreas to continue its function in an undisturbed manner. Similar conditions are occasionally encountered in other organs affected by growths (stomach, kidney, etc.).

4. Duodenal contents persistently revealing neither bile nor evidences of pancreatic secretion speak for a mechanical obstacle just above Vater's papilla (usually stone), as shown by Case B.

The clinical value of the direct examination of the duodenal contents in gall-bladder and pancreatic affections is therefore apparent. It will not be amiss to add a few lines with regard to the procedure.

PREPARATION OF THE PATIENT. The best way to obtain the duodenal contents for examination of bile is either to have the patient in the fasting condition, having inserted the tube before retiring, or else about a half-hour after the ingestion of a cup of tea with sugar or clear bouillon, the patient having taken the duodenal tube early in the morning a few hours previous to the examination.

For the examination of the pancreatic juice the same method of preparation of the patient may be applied, or any liquid diet (milk, bouillon, raw eggs), about 200 c.c., administered one to two hours previously.

METHOD OF OBTAINING THE DUODENAL CONTENTS. This is usually done by aspiration. It should be performed carefully, aspirating slowly with the syringe every minute or so, with frequent intermissions.

In case the aspiration has been performed five to ten minutes and nothing has yet appeared, two means may be employed to attain the desired end: One is by the injection of secretin subcutaneously and aspirating three to five minutes later; the other consists in employing duodenal lavage. The latter is performed in the following manner: The piston of the syringe is slowly withdrawn, the empty barrel is then filled with water (blood temperature) and raised. The latter usually begins to flow into the duodenum; if it does not, slight pressure may be exerted by pushing the piston into the barrel for a half to three-quarters of a minute in order to start the flow. The piston is again withdrawn, the flow, however, continues. Before the barrel is completely empty it is quickly lowered in order to make some of the fluid return. If this fails the procedure is repeated. Admixed with the outflowing water there is usually bile present which can serve for the examination.

ABSENCE OF BILE. In our previous paper³ we had the following paragraph regarding this point: "Occasionally we obtain on aspiration of the duodenal contents at first only a clear or slightly

³ *Loc. cit*

amber-colored fluid. It is of alkaline reaction and contains the pancreatic ferments. Usually after waiting a short time, and after repeated aspirations, a golden-yellow fluid (containing bile) appears. This has no diagnostic significance. If, however, after patient waiting and aspirating only pancreatic juice but no trace of bile appears it may be of some importance, particularly in cases of chronic jaundice. If bile is present in the duodenal contents a complete occlusion of the common bile-duct can be excluded. If the bile is entirely missing and pancreatic juice is present it points to the seat of the obstruction above the common duct."

I would like to add that absence of both bile and pancreatic juice, as already stated above, speaks for a mechanical obstruction of the common duct just above Vater's papilla, thus blocking the entrance into the duodenum of either bile or pancreatic juice (Case B.). In these instances it is advisable to ascertain positively the position of the capsule end of the tube in the duodenum by the milk test or Roentgen rays, as there is otherwise very little to go by. In one case of probable neoplasm of the pancreas with secondary involvement of the liver, not mentioned in the table, there could be found no bile in the duodenal contents after systematic aspiration, while the duodenal bucket left in the digestive tract overnight returned filled with bile, the thread likewise showing bile for several inches near the bucket. There was no jaundice present. It is difficult to explain this occurrence. Possibly the tumor in the standing or sitting postures of the patient interfered with the outflow of bile while the obstacle did not exist in the recumbent position.

DISSEMINATED SCLEROSIS.

ITS FREQUENCY COMPARED WITH OTHER ORGANIC DISEASES; ITS
ETIOLOGY AND PATHOGENESIS; THE TYPES AND DIFFERENTIAL
DIAGNOSIS OF THE DISEASE; ITS COURSE AND TREATMENT.

A CLINICAL STUDY OF NINETY-ONE CASES.

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DISSEMINATED sclerosis, or insular sclerosis, is a disorder which is still rarely diagnosed in this country. Nevertheless, omitting the syphilitic and parasyphilitic processes, it is the most common organic nervous disease. Byron Bramwell made the diagnosis

100 times in the examination of 5825 cases; Bruns, 70 times in 5500 cases; Williamson, of Manchester, 61 times in 2294 cases. In three successive years there were in the National Hospital for Paralyzed and Epileptics in London 2568 cases of nervous disease, of which 159 were diagnosed disseminated sclerosis.

On the other hand in 1902 the following statistics concerning the frequency of this disease in the private and hospital practice of American physicians were revealed before the New York Neurological Society:

Dana: 3000 cases (private), disseminated sclerosis, 10 cases.

Dana: 600 cases (clinic), disseminated sclerosis, 2 cases; in Bellevue, 12,000 general cases annually, disseminated sclerosis, 2 cases yearly.

Collins: 5508 cases (clinic), disseminated sclerosis, 18 cases.

Sachs: 2000 cases, disseminated sclerosis, 15 cases.

Starr: 10,056 cases, disseminated sclerosis, 27 cases.

Fränkel: In Montefiori Home in ten years, disseminated sclerosis, 18 cases.

Such statistics and others that one of us cited in detail in a paper before the Association of American Physicians in 1906 would seem to show that the disease is three or four times more frequent in Europe than it is in this country. This seems paradoxical, inasmuch as the majority of our patients seen in dispensaries and hospitals are Europeans.

In the course of examination of approximately 12,000 individuals presenting themselves as subjects of nervous diseases in private, dispensary, and hospital practice we personally have encountered disseminated sclerosis 91 times. It becomes necessary to believe, therefore, that the process is actually more common in Europe than here, but we think that this alone does not explain the extraordinary discrepancy. We believe that here the diagnosis is not made generally unless the patient presents a majority of the symptoms which constitute the classical form of the disease, whereas in Europe the diagnosis is frequently ventured even though none of the classical symptoms or signs is evident.

Despite the careful study of disseminated sclerosis that has been made, especially in Germany and Great Britain, absolutely nothing is known of its causation. In isolated instances it seems to stand in relationship to infectious diseases, to exposure, exhaustion, trauma, and other environmental circumstances. Such factors, however, act probably only by exciting some preëxisting constitutional tendency into activity, or by favoring the activity of some unknown metabolic or infectious toxin. We throw no light upon this question; few of our cases have come to the autopsy table, so we have no pathological findings to report. Our paper deals with the clinical observation of 91 cases in which after careful deliberation the diagnosis of disseminated sclerosis was made.

ETIOLOGY. The age of onset has been recorded in 85 of our cases: 10 (12 per cent.) occurred before the sixteenth year; 65 (76 per cent.) occurred between the sixteenth and thirty-fifth years; 10 (12 per cent.) occurred between thirty-five and forty-three; 88 per cent. occurred before the thirty-fifth year, almost the exact percentage of Bramwell's 110 cases (85 per cent.). The process unquestionably makes itself evident most commonly in youth and in early adult life. We have observed but 3 cases occurring before the tenth year where the diagnosis was ventured, though in none of these was the evidence conclusive. Totski claims to have found it present before the age of six in 19 cases, and other competent observers have recorded cases occurring in early childhood. The diagnosis in these early cases can scarcely be made with certainty, however. Only their subsequent career, their course and development, or the findings at necropsy can establish the diagnosis.

Heredity as a factor was not noted in any of our cases. It is not improbable, however, that close and systematic examination would have revealed neuropathic foundations in many of them. Reynolds has reported two instances in which the familial or hereditary factors were of great significance. In the first instance three children of a family developed the disease in the thirtieth, thirty-seventh, and thirtieth years respectively. In the second instance two sisters displayed the disease, one in her twenty-fifth year and the other in her twenty-ninth. Mettler reported one case of a man, aged thirty-two years, with fully developed evidences of disseminated sclerosis, whose paternal grandparents were first cousins and congenital deaf-mutes. The patient himself was the weaker of twins. Klausner reporting 126 cases of the disease found 31 in which heredity undoubtedly played a role; 28 of our patients were native-born Americans, 13 were British, 20 were Russian Jews, 13 were of scattered nationality; 60 per cent. were unmarried; males made up 57 per cent., females 43 per cent.

CAUSATIVE FACTORS. 1. *Occupation.* In our cases we have found such great diversity of occupation that we cannot conceive any relationship between occupation and the development of the disease. Oppenheim lays great stress upon this etiological factor. He particularly insists that metal workers and machinists are prone to develop disseminated sclerosis, and he believes that metallic poisons produce the disease. If his assumptions were correct, however, we should expect to find disseminated sclerosis much more frequently than we do among this class of workmen. We should also have to attribute almost a specific action to such metallic poisons, and we might be permitted to assume that it played a part in the development of all cases irrespective of occupation; 4 of our cases were machinists and brass-workers and 4 were jewelers working in brass, gold, and silver. On the other

hand 18 were women whose activities were confined solely to the home; 7 were school-children; 13 were clerks, stenographers, actors, etc., and the remainder had various occupations. It is reasonable to believe that occupation, like exposure, fever, and environmental factors, occasionally plays the part of activator of the disease which until then had lain dormant.

2. *Trauma*. Much the same may be said of trauma. Many observers insist that accidents and injuries are responsible for the disease. In only 4 of our cases could any such relationship be established. Recently the probable role that trauma plays in the development of the disease has become very important, because of the question of liability in accidents and their consequences. Pickenbach cites a case that illustrates this:

A man, aged forty years, on leaving his work tripped down stairs and struck his right arm, tearing or straining some muscles. Examination after four months' treatment revealed limitation of active and passive shoulder movements and atrophy of the shoulder-blade muscles. No other injuries or damages were mentioned at this time. For two months massage, passive motion, and electricity were employed, after which he was considered partially capable of performing work. Three years later he made claim against his industrial insurance company because of incapacity in working on account of pain in the shoulder. The testimony of a specialist accompanied the claim and showed the subjective as well as the objective signs of a chronic spinal disease, evidently disseminated sclerosis, that left the patient totally unfitted for work. The argument in the case naturally was whether or not the accident of two years previous was responsible for the development of the spinal disease. Pickenbach believed that there was no relationship between the two: (1) because the patient had not injured his skull or his spine, and (2) because two years had elapsed before the symptoms of the nervous disease showed themselves. He was not inclined to consider the shoulder muscle atrophies as due to anything else than the shoulder injury. Perhaps the suprascapular nerve had been torn at the time. He is unable to understand how an ascending peripheral neuritis could bring about a central nervous system disorder unless there were already present other conditions that would permit of the development of decided changes in the nerve cells.

He goes on record as saying that he agrees with Kienboeck, Kurt Mendel and Schuster, Vulpius and Ewald, who believe that the development of a spinal disease after trauma is very rare, and that heretofore too much importance has been placed upon trauma as an agent in exciting the latent disease into activity or in aggravating an already existing central nervous system disorder. Vulpius and Ewald further come to the conclusion that pathologic-anatomical processes of central nervous system diseases

cannot be influenced by a peripheral trauma. There is no ascending neuritis.

In some instances the trauma may have resulted because of the unsteadiness or insecurity due to an already existing disseminated sclerosis. There is no doubt, however, that trauma may introduce the disease. Frequently after the lapse of a few weeks or even a few days after the injury the suggestive signs and symptoms of disseminated sclerosis appear. Marburg suggests that there may have occurred a molecular or vascular damage in the central nervous system; that the delicate lymphatic walls have been lacerated, and that perhaps even minute hemorrhages have occurred. Nothing definite is known about this, however; attempts have been made to reproduce the condition by experimental trauma, but they have never been successful.

3. *Fatigue, Cold, and Exposure.* Exposure, wettings, and chills have been generally accepted as closely related to the development of disseminated sclerosis. Krafft-Ebing considers refrigeration one of the most significant factors in the etiology of the disease. Leyden and Goldschneider concur in this belief. Oppenheim, Cassirer, and Finkelburg believe that the nervous disease may be awakened by a chill or wetting. E. Müller attributes no close relationship between refrigeration or trauma and the disease, but he admits that it may play some role. Eichhorst states that "the actual significance of cold or wetting is not known, nevertheless there exists not a small number of cases of disseminated sclerosis in which this factor is the only one to be considered."

4. *Intoxications and Infectious Diseases.* Oppenheim is the champion of the view that metallic poisons play some part in the production of the disease. He found lead the commonest of these agents. Cases have been reported where zinc, mercury, copper, and other metals seem to be concerned in the production and development of the disorder. The intimacy of the relationship of such factors as these may be strikingly illustrated by the case reported by G. Etienne. Eight days after having been found unconscious from the inhalation of carbon monoxide the patient, a man, aged thirty years, developed paresthesias, and subsequently all the signs and symptoms of disseminated sclerosis.

The role of the infectious diseases in the production of disseminated sclerosis is well recognized. Typhoid fever, measles, scarlatina, diphtheria and pertussis have all been regarded as important etiological factors. The same is true for influenza, malaria, and rheumatism.

In none of our cases have we been able to detect an infectious disease as the causative or exciting agent. While many of our patients had experienced various infectious disorders in their infancy and childhood, in most cases years had elapsed before the first sign of the nervous disease appeared.

A well-known fact which we can corroborate is that syphilis appears to play no role whatever in the etiology of the disease. That hereditary syphilis is responsible for some cases, as Moncorvo suspects, we have never had the opportunity of observing.

5. *Physiological Causes* (Menstruation, Pregnancy, and Parturition). These events, always associated with more or less trauma, unquestionably have an important place in the etiology of disseminated sclerosis. Even puberty, with its lesser damages, has been considered responsible for the disease in a few cases.

We have not been able to fasten the responsibility for the production of the disease nor for its aggravation upon any of these factors, however. We cannot believe such events cause the disease, nor can we believe that they or the occupations, trauma, infections, and all other exogenous factors play a more important role than that of releasing a dormant or hitherto quiescent process. That some exogenous factor may be discovered eventually, proved specifically responsible for this peculiar pathological condition, is possible though problematical. At present we have not the slightest clue as to its nature.

PATHOLOGY AND PATHOGENESIS. The sclerotic areas may be few or many in number, irregularly distributed throughout the entire central nervous system, the nerve roots and nerve trunks. Even in cases where the symptoms suggest the involvement of a limited or localized area of the brain or cord smaller and milder patches are discovered disseminated throughout the cerebrospinal structures. Erb has stated his belief that a strictly cerebral or spinal type of the disease is very uncommon.

The patches appear as irregular but sharply outlined islets of a translucent grayish-red color. This color, contour, and consistency depend upon the age of the patch. In recent cases they are translucent, gray or gray-brown, soft and gelatinous, while in older cases they are glistening and firm to the touch. They vary greatly in size, from minute affairs that can scarcely be discovered without magnifications to enormous ones in which the area may be several square inches.

The distribution of the lesions has been the subject for study by many observers during the past few years, and several important facts have been brought out. For example it had always been generally considered that the pathological process confined itself, as a rule, to the central nervous system proper, the structures in which glia was a constituent. Now, however, careful study of the changes in the peripheral nervous system reveals the fact that it, too, may be attacked. Practically all the cranial nerves have been found affected; changes have been observed in the spinal roots and even in the trunks of the nerves.

Recent investigations have endorsed the views of many older observers that certain sites are more frequently attacked by the

disease than others. Many years ago Charcot stated that the lesions were more numerous in the white matter; that they display a preference for the ventricle walls and for the intraspinal but not the extraspinal portions of the nerves. Erb found the centrum ovale, the walls of the lateral ventricles, in fact of the entire ventricular system, and the white columns of the cord the favorite seats of the disorder. Strümpell, Gowers, and Risien Russell have endorsed these views. The old belief of Charcot that the cerebral and cerebellar cortex were rarely attacked has been maintained to the present day. Gowers believes that the process never begins in the gray structures, though occasionally it invades these. Risien Russell calls attention to the fact that though the cortical gray is only infrequently the seat of the process the gray matter of the basal ganglia is a favorite locality for it.

These observations would seem to support the view we hold, with others, that the structures bathed by the cerebrospinal fluid are the ones attacked. Tredgold recently has stated that the patches "are most plentiful in that portion of the centrum ovale adjacent to the lateral ventricles; indeed, in many cases they are in contact with and seem to extend inward from the ventricular walls precisely as they do in the cord from the fissures." Shoyer from his interesting anatomical study of two cases of disseminated sclerosis arranges the sites of the process in the cord as follows: (1) about the posterior fissures; (2) about the anterior fissures; (3) about the central canal; (4) about the entry and exit of the roots; (5) about a point in the lateral margins of the cord. He assumes that these are produced by a poisonous agent conveyed by the cerebrospinal fluid.

The work of S. P. Kramer upon the circulation of the cerebrospinal fluid unconsciously supports this view. He has injected stain into various localities of the cerebrospinal system of the living dog, and has demonstrated "the long-known though often forgotten fact that the subarachnoid cavity does not extend over the cerebral hemispheres." When methylene blue is injected into the subdural space over the cerebral cortex it remains confined to that portion of the brain above the tentorium. When it is injected under the dura in the cerebellar region the entire surface of the cerebellum, pons, bulb, upper cord, the base of the brain, and the cranial nerve sheaths are stained. When, however, the injection is made into the subarachnoid cavity of the spine the following structures are stained: (1) the outer surface of the cord in the vicinity of the injection site; (2) the lower end of the spinal cord; (3) the structures about the central canal of the spinal cord, fourth ventricle, aqueduct, and lateral ventricles; (4) the cerebellum; and (5) the sheaths of the cranial nerves. Kramer's experiments seem to prove conclusively that the direction of the current of the spinal fluid in the subarachnoid is downward, then into the ventricular system,

entering the cerebrospinal canal somewhere near the termination of the cord, then ascending the canal to the fourth ventricle, and through the aqueduct to the lateral ventricles. Such a circulating medium appears to have nothing to do with the surface of the cerebral cortex. Furthermore, the spinal nerve roots outside the dura are not stained, so there is evidently no lymph connection between the spinal subarachnoid space and the nerve sheaths. Assuming, therefore, that the poisonous agent circulates in the spinal fluid it is reasonable to believe that only these structures washed by the fluid become the sites of the diseased process.

Microscopic study of the acute patches reveals characteristic changes in the sheaths and in the axis-cylinders themselves. The diseased patch is usually sharply defined or delimited from the surrounding healthy structures. The border, however, may be less involved than the centre. E. W. Taylor has described patches in which there was no such border or intermediate zone; there was abrupt transition from the diseased to the healthy tissue.

In the border there may be observed various degrees of disturbance to the sheaths and axis-cylinders. The sheaths may be swollen, irregular, and knobby, while phagocytic cells may be observed plentifully, carrying away the products of fatty degeneration to the perivascular lymph spaces. Such spaces are often crowded with lymphocytes, leukocytes, and plasma cells, suggesting a distinct inflammatory reaction.

The axis-cylinders evidently are more resistant than the sheaths to the action of the toxic agent. Patches have frequently been described in which the sheaths had disappeared entirely, leaving the axis-cylinders intact. For a number of years this was considered the peculiar hall-mark of the pathological process, and even today, when we know that these axis-cylinders eventually are destroyed, we regard this peculiar resistance as characteristic of disseminated sclerosis.

The changes occurring in the axis-cylinders have been carefully studied and prove to be similar in character to those observed in the sheaths. They become swollen and lose their capacity for staining clearly; they become thin and spiriform; they show fusiform thickening. Definite disintegrative changes occur in certain portions of the axis-cylinder while other portions of the same fiber remain normal. The fibrils may remain intact even though the axis-cylinders are intensely swollen, but they too finally succumb.

These phenomena accompanied by vascular changes are regarded by Gombault as a "periaxial neuritis." The acute patches produced in this manner and the subsequent changes, chiefly glial and vascular in character, are defined by Marburg as "encephalomyelitis periaxialis scleroticans." His views are in the main held by G. Oppenheim, Tredgold, Lejonne and Hermitte, Maasz, Risien Russell, and others. The actual sclerotic phase occurs probably

after the acute condition. With the removal of the degenerated products by the phagocytes, numerous spaces or interstices are left, giving the patch its "areolated" appearance as Redlich describes it. It is at this time that the glia proliferation attracts attention. Previous to this time no increase in fibrillar structure can be observed, though there may be proliferation of the glia cells. At times a scarcely visible webbing of young neuroglia can be discerned woven throughout the affected parts. Eventually there is a heavy glial growth and a thick fibrillar network is formed. Dense masses of interstitial tissue are found running parallel to the involved fibers in the patch. When the gray structures are affected a thick mesh composed of small glial cells and fibrils is seen branching in all directions from the denser and older centre. An ancient patch in which the glia has shrunk, and in which various changes in the vessel walls may have occurred, generally exhibits profound destruction to the axons and sheaths. It is only rarely the case that the axis-cylinders persist throughout this stage of glia proliferation, though this may actually occur.

Much discussion has arisen concerning the condition of the bloodvessels in the diseased patches. Many observers have found no significant changes, while others have described every degree of involvement of the vessel walls from simple nuclear increase and scarcely noticeable thickening to the densest thickening with hyaline degeneration and occlusion of the lumen.

What remains the most perplexing feature after all, however, is the absence of secondary degeneration in the involved tracts. Schultze has endeavored to explain this as due to the integrity of the axis-cylinders; that as long as they remained functional secondary degeneration would not occur. At present, however, we know that even with total focal destruction of the nerve fibers, sheath, and axis-cylinders there may be no secondary degeneration. Marinesco and Minea recently offered an interesting explanation concerning this phenomenon. They believe that systemic degeneration occurs, but that the degenerated fibers are absorbed and therefore are not to be observed. This idea is supported by the observations of others who have been able to note individual fibers in the columns, undoubtedly showing degenerative changes. Still others have recorded cases where the degeneration of entire tracts was pronounced.

THE CHARACTER AND ORIGIN OF THE PATHOLOGICAL PROCESS. We know no definite or adequate explanation of the nature of the process. The essential question of which structure is primarily involved has never been answered. If we possessed such information we should soon after, in all probability, discover the nature of the diseased process. The four well-known hypotheses concerning this problem are still with us and each has its supporters.

1. *The Parenchymal Theory* (Adamkiewicz, Huber, Redlich, Richien Russell, Borst, Thomas, and others). The neurons themselves are initially involved. Through the action of a toxic agent circulating in the blood or the cerebrospinal fluid there occurs focal destruction of the sheaths and axis-cylinders. Subsequently there is secondary proliferation of the glia, and eventually structural vascular changes may develop. New evidence has recently been offered (Siemerling and Raecke) which appears to support the idea that the process is a definite parenchymatous inflammation inaugurated by capillary hemorrhages.

2. *The Interstitial Theory* (Charcot, Leyden, Wernicke, Erb, Goldschneider, Gowers, and others). This is the oldest of the views, and it is summed up by Charcot's definition "a primary and multilocular chronic interstitial myelitis or encephalitis." The interstitial tissue is the initial seat of the pathological process; the changes in the parenchyma are secondary. Leyden and Goldschneider are of the opinion that the whole process is a type of chronic myelitis.

3. *The Multiple Gliosis Theory*. Strümpell regarded the disorder as a multiple gliosis, owing its existence to some congenital or inherited tendency to proliferation of this tissue. Here too the glia is the initial structure implicated, but the disorder is not inflammatory in character. Strümpell compares the disease to multiple neuroma, lipoma, and others in which congenital influences evidently play an important role. This hypothesis is the only one which assumes an endogenous cause for the disease. Such an inherited tendency may be alone sufficient, but exogenous influences may give the impetus to development of the process. E. Müller and Byron Bramwell support Strümpell's idea.

4. *The Vascular Theory* (Rindfleisch, P. Marie, Ribbert, Bastian Popoff, Buss, Hess, Williamson, and others). This theory attributes the disease to a primary disorder of the bloodvessels, with secondary changes in the parenchymal and interstitial tissues. Tredgold rejects it, saying that local areas of necrosis as a result of vascular disease have not the sharp, punched-out appearance of those in disseminated sclerosis. As a matter of fact, vascular changes are rarely prominent in this disease, while they are pronounced in definite vascular disease such as syphilitic endarteritis. In many cases of disseminated sclerosis no vascular changes whatsoever are to be found.

Notwithstanding the fact that knowledge concerning the origin of the disease is quite indefinite, we are ready to accept the view that it is essentially a parenchymatous degeneration produced by a toxic agent. Whether this be a degenerative process from the very beginning or whether it be preceded by an actual inflammation remains to be discovered.

TYPES OF THE DISEASE. On attempting to classify types of the disease we meet with considerable difficulty. Our classification must be either anatomical, physiological, or clinical, and none of these lends itself to definite division. That is to say, we can no longer speak of a cerebral, a cerebellar, or a spinal type unless we mean that the intense or the pronounced damage has evidently occurred in these localities, although we recognize evidences of lesser involvement elsewhere. It is exceptional that these localities are affected alone; the disease is now regarded as a general one in which the lesions are scattered throughout the cerebrospinal system. The same difficulty is encountered on attempting to group the cases from a physiological stand-point. Should we speak of a "spastic-parietic," or an "ataxic," or "hemiplegic" form of the disease we must bear in mind that only rarely do these disturbances occur, uncomplicated by symptoms of involvement elsewhere.

Nevertheless, both of these classifications, inaccurate as they must be, are not without value to us, for they reveal the widespread distribution of the process, on the one hand, and the great variety of symptoms on the other.

Depending upon the site and the intensity of the lesion, practically every symptom of involvement of the nervous system may occur. They may be so slight that their existence may remain unrecognized for months; the patient himself may be unaware of them or he may disregard them. Minor disturbances of muscular power, a tendency to fatigue too readily, a slight incoördination or loss of skill, may not excite his attention until they tend to incapacitate him. This is true, likewise, of the sensory disturbances, paresthesias, blurred and double vision, headache and dizziness, and many others, particularly when they are of temporary and short duration.

On the other hand the disorder may be introduced without the slightest warning by a complete and sudden apoplectiform hemiplegia, which may be accompanied by aphasia.

We have found in the large majority of our cases that the earliest manifestation was weariness and weakness in the legs. The patients describe this "leg weariness" as a feeling of heaviness in the feet and an abnormally early tiring and fatigue. Frequently there is associated a weakness of the bladder; there is inability to hold the urine as well as usual, and there may be urinary incontinence at times. Invariably when the patients presented themselves there was already established an involvement of the motor mechanism of the legs and bladder, which varied from a mild spasticity to a totally incapacitating spastic paralysis. It is quite extraordinary that we report eighty-three of our cases of this type, not one in which the arms were involved in a similar manner. And equally remarkable is the fact that we have never encountered a case in which the paralysis was of the lower neuron type.

The variability in the manner of development is as great as that of its intensity and impairment. For a long time, perhaps years, there may be no subjective manifestations. Not infrequently the patient tells of occasional cramps in the legs or a "drawing up" of the legs at night. There may be but slightly disordered gait, due to a characteristic stiffness which, in severer form, may be associated with weakness and unsteadiness. In other cases the gait may be profoundly impaired and in a short time locomotion may become impossible. Under such circumstances the rigidity may be extreme and the patient becomes unable to lift the feet from the floor because of flexor spasm. Eventually, unable to stand, he becomes the bed-ridden victim of flexor and adductor contractures.

The bladder and rectal sphincters seldom escape in disseminated sclerosis of this type. Here again all degrees of impairment are met with, although, as a rule, they are slight in the beginning and are due to hypertonicity. The earliest difficulty is the inability to retain the urine for any considerable time; it becomes imperative to release the bladder upon its earliest demands. Retention often occurs and the spastic contraction of the sphincter may be sufficient to prevent the entrance of a catheter into the bladder. In later stages and in fully developed cases of the lower spinal type of the disease incontinence is present practically always. Involvement of the rectal musculature occurs much less frequently.

Disorders of the cutaneous sensory mechanism were present in less than 10 per cent. of our cases. Most of these were subjective feelings of numbness and tingling in the extremities. Pain as a symptom was rarely encountered. It is an interesting fact, in accord with most writers, that the shooting pains and other crises so common in tabes practically never occur. Objective sensory disturbances were discovered very rarely, and even in those cases where paresthesias were pronounced it was the exception to find noticeable defects in the acuteness of the cutaneous sensibility. Cases occur, however, where there is marked sensory disorder in the hands and feet. Deeper sensibility was impaired in very few of the cases seen by us. Astereognosis was recorded in four of them.

We wish, therefore, to classify a group of cases of disseminated sclerosis which was by far the commonest in our series as the spastic type; characterized by hypertonic paresis or paralysis of the legs, usually accompanied by bladder weakness, and, infrequently, by disturbances of the cutaneous and deep sensibility. Quite often no other signs were present, but usually there were evidences of involvement of other parts of the nervous system. Nevertheless the characteristic impairment was the involvement of the legs and bladder. This permits of a convenient clinical grouping; 65 per cent. of our cases come under this division.

A second type of the disease may be considered as the ataxic.

Here the dominating feature is the incoördination or unsteadiness due to ataxia and tremor. Arbitrarily we may place in this group those cases in which the chief disorder is ataxia, vertigo, intention tremor, scanning speech, and nystagmus. These symptoms rarely occur singly. Usually they are all present in the same case, and quite often they are accompanied by manifestations of more or less severity due to involvement of the spinal cord. This is the cerebellar form of disseminated sclerosis; 25 per cent. of our cases were of this group, which approaches the classical type of the disease described by Charcot.

Ataxia is not infrequently the initial symptom of bulbar and cervical involvement. Such cases may simulate tabes dorsalis; the disordered gait and station may be identical with that of tabes because of involvement of the kinesthetic pathway. More commonly, however, the ataxia is of the cerebellar type, uninfluenced by vision; that is to say, it is not made worse by closure of the eyes.

Intention tremor is more frequently encountered. The nature of this characteristic symptom has given rise to considerable speculation, particularly concerning its relation to ataxia. At times the tremor becomes so pronounced that it results in marked incoördination. Strümpell considers it a genuine ataxia and Risien Russell believes it is due to "a failure of synergic action of muscles in purposive movements, consequent on an unequal degree of innervation both of the muscles directly concerned and of their antagonists." The tremor usually accompanies movement and is seen, therefore, more commonly in the eyes (nystagmus), head, and hands. It is well known, of course, that it becomes most pronounced on effort or fixation and in muscles that have been previously fatigued. The innervation of the trunk muscles is quite frequently affected and the station and gait may be profoundly disordered by this asynergia alone.

A great variety of speech defects have been described. These range from the slightly monotonous speech (bradyphasia) to disturbances which are truly ataxic. The characteristic disorder, however, is the slow, scanning, syllabic speech due to abnormal intervals between the words and even between the syllables. The cause of this is an unusually rapid fatigue of the speech and respiratory muscles and an inability to adjust perfectly the relation between the action of the expiratory muscles and those of the larynx. This rapidly developing weariness and fatigue is well illustrated in one of our cases:

Patient is M. B., a young girl, unable to speak any considerable sequence of words because of loss of power. She is also unable to hold her breath after a full inspiration for more than a few seconds. In attempting to sing any moderately high tone she can sound it, but it exhausts almost at once. These disorders, in addition to

a slight oscillatory nystagmus, were the only symptoms present; nevertheless, we feel justified in regarding them as evidence of a beginning disseminated sclerosis.

Very rarely the speech becomes almost entirely disorganized. It may be of a paralytic character, and when accompanied by disturbances in coördination of the swallowing, breathing, and heart mechanism may be considered due to a lesion in the bulb.

Nystagmus may be considered as fundamentally a fatigue phenomenon, due to an incapacity for even slightly sustained effort, because of abnormally quick fatigue (Ulthoff, Marie, Strümpell). Essentially also it is an intention tremor (Charcot), similar to those we have been describing. We shall discuss nystagmus more in detail in a subsequent part of this paper.

The third group is characterized by hemiplegia of evident cerebral origin, identical with that occurring as the result of the occlusion of a cerebral artery. This hemiplegic type occurs relatively infrequently. Developing gradually, as a rule, but at other times with apoplectic suddenness a paralysis of one side of the body occurs, varying in intensity from a slight weakness and loss of skill in performing fine movements to complete incapacity. Such a disorder due to disseminated sclerosis is usually described as of fleeting character. After a few weeks or even after a few days the function may be restored in large part or completely. Our cases (7 per cent. of the series) were not so fortunate. Months and years elapsed yet no improvement took place.

Again it becomes necessary to remark that the hemiplegia may exist alone. No other characteristic evidence of disseminated sclerosis need necessarily be present, especially if the disease is being introduced in this fashion. The paralysis may develop overnight in an individual otherwise apparently normal. The subsequent career of the case is necessary, as a rule, before a definite diagnosis may be permitted. More usually the hemiplegia arises in cases that had been recognized previously as disseminated sclerosis, or which upon subsequent examination show significant signs of involvement of other parts of the nervous system. An instructive illustration of the hemiplegic form of the disease is the following case:

A strong, well-developed girl, aged nineteen years, a champion swimmer, noticed a progressing awkwardness in her hands, which had been preceded for two months by a painful coldness in the hands. She dropped articles from her hands when her visual attention was not directed upon holding them.

Her previous history was negative except for two accidents from which she apparently fully recovered. When sixteen years old she struck her head while diving and immediately felt a "pins-and-needles" sensation down her spine, but no apparent damage was done. During her seventeenth year she was knocked senseless

in a basket-ball game and felt too ill to attend school the following day, but was soon as well as ever.

Soon after the disability in her hands, weakness of the left leg developed so that it dragged in walking. She suffered also from an acute coldness in all the extremities. At the same time it was observed that she did not fully appreciate pin-pricks in the hands and arms. Three months later she became irritable, emotional, and unable to walk or stand. After seven weeks in bed she improved so much that she was able to take long walks; the left arm and hand, however, had become increasingly disabled, so that they were now stiff. After being urged she went into the ocean to swim, the idea being to increase the function of the rigid arm and hand. The result was disastrous, as there developed a rigidity of the left leg and loss of bladder control, as well as ataxia in the right arm. In short, within a period of six months a vigorous athletic girl had developed a hemiplegia which has persisted to the present time, a period of three years. Her mentality is good but she is emotionally unstable. In speaking, words flow faster and faster, so that at the end of a statement there is an explosion of sound accompanied by exaggerated movements of the face and irregular movements of the right arm. The spinal fluid is normal.

As a matter of convenience we shall now consider the signs and symptoms of involvement of other parts of the cerebrum and the cranial nerves. This includes psychic disorders as well as disturbances of the optic and auditory pathways. Disseminated sclerosis may exist without any of these, particularly when the pathological process is confined largely to the spine and bulb. As a rule they are present, more or less prominently, in all cases where the cerebrum and cerebellum chiefly are affected, and this is particularly true of involvement of the optic tract.

Ocular Phenomena. The recognition of the changes occurring in the visual apparatus is of the utmost importance in the matter of diagnosis. It not infrequently happens that they may be the only manifestations of the disease for months and even years before other characteristic signs appear elsewhere. Windmüller, for example, records a case in which acute retrobulbar neuritis occurred seven years before any other symptoms could be distinguished. Moreover the ocular changes are among the commonest of the diseases, as Uhthoff has disclosed, and they may be considered almost characteristic or at least strongly corroborative of disseminated sclerosis alone. The most typical are the changes that occur in the acuity of vision, the disorders of the visual fields, and the alterations in the appearance of the disks.

Visual Acuity. A slight blurring of vision with occasional flashes of light before the eyes may be the earliest manifestation of the disease. As a rule this is only a transient process which may not reappear for weeks or months. It usually remains confined to

one eye, and it may or it may not be accompanied by changes in the disks. This tendency to improvement and relapse has long been regarded as peculiarly characteristic of disseminated sclerosis. There may be defective vision for months, limited, perhaps, to one eye, followed by a period lasting for months, during which there is apparently normal vision, then eventually the return of the disorder to the same eye, the other eye, or both of them.

The onset may be gradual and scarcely appreciated by the patient. More frequently it announces itself suddenly in almost complete blindness. Even in such cases remissions occur lasting variable lengths of time. This peculiar quality of the symptoms need not necessarily be present in every case, however; 21 per cent. of our cases had ocular symptoms, but in not one of them could a history of remission be obtained.

Visual Fields. The essential cause of the amblyopia and the disorders of the visual fields is considered to be a sclerotic patch in the optic nerve, commissure, or tract. This is contrary to the older view of Gowers, who regarded the optic atrophy as the result of a primary degeneration of the nerve elements similar to that which occurs in tabes. The more recent evidence supports the idea that the pathological process is a retrobulbar neuritis which results in more or less destruction of the nerve elements. We should expect early manifestations of involvement of the macular fibers, therefore, and this actually occurs. Central scotoma is a prominent and common disturbance in disseminated sclerosis. Uhthoff observed it in 15 of his 20 cases; Klingman, recently, in 11 of 14 cases.

The occurrence of retrobulbar neuritis in any case, but especially in the young, should at once excite suspicions of disseminated sclerosis. It is an acute process, as a rule, giving rise to damaged vision and central scotoma which show a tendency to improvement. Nicotin, alcohol, and syphilis have commonly been blamed heretofore, but in many cases it has been impossible to establish any relationship between the disorder and these agents. Such cases of so-called "idiopathic retrobulbar neuritis" have recently been studied by Fleischer, who regards them as early manifestations of disseminated sclerosis. Schultze, furthermore, examined cases in which tobacco, alcohol, and syphilis had been considered the causes and found unmistakable evidences of disseminated sclerosis in many of them.

Peripheral contraction of the visual fields, while not so common as central scotoma, occurs quite frequently. Uhthoff observed it in 11 of his 24 cases; Klingman in 11 of 14 cases.

Changes in the Disks. The characteristic change noted in the disks when the optic nerve has been implicated is atrophy. Any stage of the process may be encountered from a slight pallor of part of the disk to complete atrophy in both eyes. The entire

disk may not be equally involved. Various portions appear degenerated before others; even in the earliest stages it is well known that the temporal half is earlier affected than the nasal half. There may be a great difference in the extent of involvement of the two disks; a beginning pallor alone may exist in one eye while extensive atrophy is present in the other.

The most remarkable fact, however, concerning the changes in the disks is the discrepancy which exists between the apparent degree of atrophy and the actual disturbance of vision. Pronounced pallor of the disk may be present for months and years with practically no diminution of visual acuity. On the other hand, marked involvement of the fields and visual disorders may exist when the disks appear quite normal. This peculiar lack of parallelism between the structural damage and the functional incapacity is unique with disseminated sclerosis among all the organic nervous diseases. Not only is this true on the part of the ocular apparatus, but the entire brain and cord may be the seat of extensive tissue changes disclosed by autopsy in cases whose clinical career had been extraordinarily mild.

Affections of Ocular Motility. Nystagmus when present is one of the most characteristic symptoms of disseminated sclerosis. It is one of the original triad of symptoms of the classical types of the disease described by Charcot, and even now when we no longer demand its presence to distinguish the nature of the disorder we recognize it in nearly 60 per cent. of all cases.

As a rule true nystagmus appears late in the course of the disease, though "nystagmiform" jerks and twitchings may have existed before. Uhthoff, Baranyi, and Bartels would have us distinguish between the two. True nystagmus, which is oscillatory, swinging to and fro about a central point with rapid equal movements, is in all probability a fatigue phenomenon (Uhthoff, Marie, and Strümpell). It occurs independently of voluntary movement of the eyes, in changing the direction of gaze; the oscillations continue even in the resting stage. It becomes more intense, however, when the eyes are turned and attempts at fixation are made, particularly in extreme directions. At such time the "nystagmoid" movements appear. They are characterized by sharp, quick jerks in the direction of the object of fixation, with slower movements of return. These movements occur about three or four times a second and appear to be in every respect "intention tremors" (Charcot).

Uhthoff found external ophthalmoplegia well established in 17 per cent. of his cases. The sixth nerve was more frequently involved than the third or fourth. The disorder is not usually so severe, however; transient weaknesses of individual muscles are more likely to be met with, and these are scarcely ever maximal. Windmüller records ocular palsies, counting diplopia as an evidence of such in 70 per cent. of his cases.

Pupillary changes are uncommon. The reflexes are generally active, and only at times may a slight disparagement be observed between the activities of the two sides.

Auditory and Vestibular Systems. The cochlearis division of the auditory nerve is only rarely involved. The symptoms may vary from a slight acoustic hyperesthesia (E. Müller) to total deafness. O. Beck describes two cases in which he was able to diagnose disseminated sclerosis without any neurological data except the peculiar variations of the acoustic and labyrinthine functions. Excitability of the vestibular apparatus and capacity for acute hearing, determined by many tests, alternated with absence of excitability and complete deafness without revealing in the interval any of the typical signs of labyrinthine impairment. This variance between the subjective symptoms and the objective signs is similar to the condition frequently observed on the part of the visual apparatus; the coexistence of quite normal vision with marked pallor of the disk, and *vice versa*.

Unusual rapid fatigue of the acoustic mechanism determined by tuning-forks was discovered by Claude and Egger, and daily changes in acoustic keenness have been observed by Marburg.

Involvement of the vestibularis division of the auditory nerve is not uncommon. Vertigo is frequently an initial symptom of the disease. Nystagmus and its significance has been discussed previously.

Psychic Phenomena. Psychic disturbances of every variety have been observed from slight blunting of mental activity to profound dementia. They may precede the development of the more usual symptoms of disseminated sclerosis by months or years, their true nature, therefore, remaining unrecognized. It is very difficult to say how frequently mental symptoms occur as early evidence of the disease, for they may be of such slight significance as to escape notice, or so severe as to necessitate the confinement of the patient in psychiatric hospitals where it is not unlikely their true nature could only have been determined by the subsequent appearance of other characteristic evidence.

Changes in the character and disposition may occur; an unusual cheerfulness, an uncustomary tendency to laughter entirely out of proportion to the exciting cause. A distinct euphoria is common, accompanied by more or less boisterous laughter. Ten of our cases presenting mental symptoms behaved in this fashion, and they revealed, in addition, impairment of memory, judgment, observation, and attention. As a rule there was always to be observed a heightened sensitiveness or increased excitability, though in none of them did this ever become a delirium or mania.

In three cases pronounced apathy and depression were early symptoms.

COURSE AND DEVELOPMENT. Disseminated sclerosis reveals itself gradually, as a rule, developing so insidiously that it

frequently escapes observation for months. We must not lose sight of the fact, however, that it may be inaugurated abruptly, with apoplectic manifestations, although, as we have pointed out, this manner of onset is very unusual.

Once established the disease runs a chronic progressive course, during which there may be remissions and even apparently complete recovery. Most observers lay stress upon this. It has become an accepted fact that remissions are characteristic of the disease. We have no intention of disputing this; nevertheless, in our cases it has not been observed except in a few instances when slight improvement occurred. With these exceptions they were all of the chronic, progressive type of long duration. The duration of the disease is very indefinite. It is apparent, of course, that years may elapse before death, which is usually due to complications or intercurrent diseases.

Diagnosis. The recognition of the fully established Charcot case presents no very great difficulties as a rule. With all the cardinal features, or even a few of them, there is little possibility of error. Tremor, nystagmus, and incoördination defects, especially in the young, may be considered due to disseminated sclerosis, keeping in mind, however, the important reservation of cerebellar tumor or cyst. It is vitally important that we do not overlook these because of the relief now possible by early surgical intervention.

Cerebellar Tumor and Cyst. The difficulty in the differential diagnosis is dependent upon the fact that a small cerebellar cyst or a slowly expanding tumor before being able to raise the intracranial tension behaves exactly as a sclerotic patch. The difficulties may be illustrated by this case:

J. H., aged nineteen years. In June, 1912, his gait became unsteady; people believed him to be intoxicated. Two months later he began to vomit after his meals and soon began having headaches all day long. Two months later the headache and vomiting diminished in intensity, but he then became disturbed by vertigo. On examination he presented static and dynamic ataxia, tremor, slurred speech, and nystagmus. The disks seen in the early phases of the process showed clear and there was no fault in the vision. In the course of the following year the signs of increased intracranial tension revealed themselves. A definite choked disk appeared and an operation was decided upon. Cystic tumor of the right cerebellar lobe was found. The patient recovered promptly and at the time of this record has been relieved of most of his disorders.

Only one fact is of value in influencing our diagnosis and determining our course in this case: that is the presence of symptoms that must always be regarded as significant of increased intracranial tension. Headache, vomiting, and giddiness, with optic

neuritis, are not at all uncommon in disseminated sclerosis; nevertheless these must remain the exceptions, and in case of doubt, as we encountered in the case above, with such symptoms present, we dare not disregard the idea of tumor until we have disproved its existence.

The absence of spasticity is of no value one way or the other. It is true that in disseminated sclerosis we encounter spastic phenomena commonly because of involvement of spinal tracts by other sclerotic patches, and in cerebellar tumor this does not occur until by expansion pressure is exerted upon the pyramidal system.

Because of the symptoms of increased intracranial pressure we diagnosed tumor which proved to be correct.

Cerebrospinal Syphilis. Of first importance in the differential diagnosis of the less well-established and aberrant forms, particularly of the spinal or spastic-paretic type, is syphilitic pachymeningitis. The occurrence of spastic phenomena in the legs, with or without sensory and bladder disorders, is due, in the vast majority of cases, to syphilis; we have come to look upon these symptoms as more or less distinctive of this disease, and especially when a history of the infection is acknowledged. The difficulty in the differentiation is not so great in advanced cases; there is usually some corroborative evidence present, as involvement of the pupils, the cranial nerves, or, perhaps, apoplectiform attacks. Without these, especially in the early phase of the disease and without additional proof of disseminated sclerosis, we have no means of deciding unless we resort to examination of the cerebrospinal fluid.

We are in possession of valuable facts concerning the spinal fluid in nervous diseases through the important studies and contributions of Nonne, Plaut, Noguchi, Kaplan, and many others. The information obtained from serological and chemical examination of the fluid is invaluable in practically every disease of the nervous system we are called upon to treat; spinal puncture is a routine necessity in all neurological practice even when we feel secure with our clinical diagnoses.

Two laws seem already to have been established: (1) a positive Wassermann reaction in the spinal fluid, irrespective of the reaction in the blood, is absolutely certain proof of cerebrospinal syphilis; (2) in disseminated sclerosis the fluid is normal in every particular, that is to say, the Wassermann is negative, and there is no increase in the globulin or the lymphocytes.

The value of this information is at once apparent. If we recall that invariably with a cerebrospinal showing a positive Wassermann reaction we find the globulin and the cells increased, at times only slightly and at others enormously, we realize that we have a means of distinguishing between the luetic and the non-luetic spinal diseases.

Kaplan in the analysis of more than 3000 spinal fluids obtained

from patients having nervous diseases found 16 in which the diagnosis of disseminated sclerosis had been made with certainty, all of which possessed fluids normal in every particular. In cases where the differentiation was doubtful the laboratory analyses were considered sufficiently strong evidence to decide the question. When the fluid contained fifty or more cells to the cubic millimeter or an excess of globulin or a positive Wassermann reaction the diagnosis of disseminated sclerosis was excluded.

Whereas it is very common to find with a negative Wassermann in the fluid an increase of lymphocytes with or without an increase of globulin the reverse practically never occurs; that is to say, a positive Wassermann does not exist where there is neither lymphocytosis nor globulin increase. In but 6 of his 3000 analyses did he meet with this phenomenon, and all of these were cases of arterial syphilis.

Transverse Myelitis. In transverse lesions of the cord produced by localized myelitis, tumor, gumma or caries, or syringomyelia the differential diagnosis may require very careful deliberation. Myelitis develops quickly, as a rule, accompanied by fever and toxemia. Its sequelæ, spastic weakness, or paralysis of the legs and visceral and sensory disorders may be very severe and permanent, but is not progressive. Atrophy and fibrillary twitchings, frequent in transverse myelitis, are seldom encountered in disseminated sclerosis. Usually there are no cerebral symptoms in transverse myelitis.

Disorders of vision may be present, though they are unusual, and as recently pointed out by Ward Holden, lateral hemianopia for one eye alone is a symptom of considerable diagnostic value in cases in which visual disturbances precede the spinal symptoms.

Oppenheim and Cassirer have recently reported cases in which there developed quickly an acute ataxia with weakness of the upper extremities, atrophy of the intrinsic hand muscles, paresthesias, and objective sensory disturbances. They regarded the cases as acute cervical myelitis until subsequent developments proved them to be disseminated sclerosis.

Spinal Tumor. Disseminated sclerosis not infrequently gives rise to a series of symptoms suggesting spinal cord tumor. Nonne recently called attention to the difficulty which may arise in differentiating between them. Laminectomy performed in four cases of suspected tumor proved negative. Subsequently in two of these section showed disseminated sclerosis and disseminated confluent myelitis; and further progress of the other two substantiated the diagnosis of disseminated sclerosis. One of these was a youth, aged nineteen years, with symptoms of a transverse lesion of the dorsal spine. There were spastic paralysis of the legs and sensory disturbances to the ribs, with fever and slight delirium in the beginning of the disease. A laminectomy was performed, but no lesion was

discovered. In a few months decided improvement took place, and for five years the patient has been well. The history of this case is astonishingly like that of another which we had the privilege of observing on the service of Dr. Pearce Bailey. In a few months after laminectomy for suspected cord tumor had been done the patient, a splendidly developed athlete, with a profound paraplegia and bladder and sensory impairment, recovered completely; no trace of the disorder remained except an exaggeration of the knee and ankle-jerks.

Syringomyelia. Under certain circumstances, syringomyelia may resemble disseminated sclerosis, particularly as the rather characteristic dissociation of the cutaneous sensibility may occur in the latter. It has been stated also (Russell) that nystagmus may occur in syringomyelia.

In the early months of the following case the question of the existence of syringomyelia was given respectful consideration. Only with the unfolding of characteristic evidences of disseminated sclerosis was the correct diagnosis possible.

W. N., aged twenty-seven years, a draughtsman. His history is negligible. His habits excellent. He seeks relief for weakness in the right arm, numbness of the entire left side, and some slight difficulty in starting the urinary flow. These symptoms developed rather suddenly two weeks before his admission here.

Status July, 1910. Weakness of the right arm and to a lesser extent the right leg. All tendon jerks on the right are increased; ankle and wrist clonus present. Babinski reflex in right foot. All cutaneous reflexes absent on the right. Almost complete loss of cutaneous sensibility in the left half of the body from the clavicle to the toes. Wassermann negative in the blood-serum and in the spinal fluid. Patient made almost complete recovery in ten days.

Status August 22, 1910. New attack with sudden onset involving the right arm, the right leg, and the left leg. These extremities are now spastic while on both sides of the body there is complete loss of sensibility. Improvement began almost immediately. In one month the left leg was practically well; the right side improved more slowly.

Status October, 1910. Patient, who had been in good condition, suddenly became quadriplegic and lost all sensation to the level of the shoulders. Improvement began again, more slowly than before. In January, 1911, the left arm and hand were almost normal. He was also able to use the right hand quite well. Both legs still profoundly involved by a high-grade spasticity. Right and left-sided Babinski sign is present.

Status May 5, 1911. Halting, scanning speech is present now. There is also fine nystagmus apparent. Patient is depressed and irritable.

Paresis (general paralysis of the insane). There should be no longer any difficulty in differentiating between disseminated sclerosis and paresis, which it occasionally resembles. The stumbling and trembling speech of paresis with its omitted syllables and words differs fundamentally from that of disseminated sclerosis, while the mental changes of the latter are usually not so severe as of the former. In fact the objective evidences of paresis, including at the present time the characteristic cytological and chemical findings of the cerebrospinal fluid, are conclusive proofs of the disease.

Hysteria. We believe we have not encountered the difficulty, said to exist, in distinguishing between disseminated sclerosis and hysteria. The majority of authors, however, lay considerable stress upon the similarity between them. They are practically of one voice, furthermore, in saying that the difficulty generally results in mistaking an existing disseminated sclerosis for hysteria.

The two disorders are common to youth and young adult life, and both frequently develop after a physical or psychical trauma. A widespread variability of disorders is common to both of them, involving somatic, visceral, and mental functions.

The regular, concentric narrowing of the visual fields, especially with parallel contraction of the color fields, speaks for hysteria. Optic pallor and optic atrophy of hysterical nature is impossible. True nystagmus should always be considered evidence in favor of the organic disease. Sensory changes are common to both disorders, and are, of themselves, of not much importance in the differentiation. Sharply defined anesthetics and analgesias are not usually found in disseminated sclerosis and an anesthetic cornea practically never occurs. Bladder disorders are usually indicative of disseminated sclerosis, and actual exaggeration of the reflexes, especially when accompanied by a Babinski sign, must always be regarded as proof of organic nervous disease.

A sign of great importance in the diagnosis of disseminated sclerosis is the absence of the abdominal and epigastric reflexes. This was first pointed out by Strümpell, who observed it in 67 per cent. of his undoubted cases. His views have been corroborated by many observers. E. Müller and Cassirer, for example, regard the bilateral absence of these reflexes as of distinct and useful diagnostic significance. Marburg noted its absence in 38 of his 40 cases, and interprets it as an involvement of the lower third of the dorsal cord.

TREATMENT. No advance has been made in the treatment of the disease if we except radiotherapy as used by Prof. Marinesco, of Bucharest. He ventured to try this therapy because of the good effects he had observed in the use of the Röntgen rays in disseminated sclerosis and syringomyelia. He described unquestionable improvement in the tremors, the weakness, and the fatigability. Rays of 1 milliamperè intensity were applied for seven to ten

minutes to the lumbar spine. No skin irritation or other complication ensued. We scarcely dare place any great hope in the agent, however, when we recall the nature of the pathological process. We must remember, too, that the improvements we may attribute to the action of the remedy may occur spontaneously.

In the meantime it is well to bear in mind the good advice of Oppenheim and Müller, that rest is essential; all fatigue is to be avoided, and only moderate exercise to be permitted. Gentle massage and sedative baths may be appreciated.

RESUMÉ. Disseminated sclerosis is encountered much less frequently in this country than abroad. This is due, in part only, to the fact that early and irregular cases frequently escape recognition here.

The fully developed, classical Charcot type of the disease is rarely seen.

Trauma, including occupation, injury, intoxications, biological crises, mental shocks, etc., play only a contributing role in the development of the disorder.

The disease is regarded by us to be a parenchymatous degeneration due to the action of a toxin circulating in the cerebrospinal fluid.

There can be no rigid grouping of "types" of the disease. Nevertheless three general groups can be assumed: a spastic-paretic, an ataxic, and a hemiplegic group.

The best single aid in the differential diagnosis is the condition of the cerebrospinal fluid. The Wassermann reaction is practically always negative. The number of lymphocytes is less than fifteen, and there is no excess of globulin. This is of special value in ruling out cerebrospinal syphilis.

The remissions which sometimes occur are singularly characteristic of this disease. In our series, however, they were rarely encountered.

The absence of the abdominal reflexes, upper and lower, is an important diagnostic sign.

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A CASE OF SPRENGEL'S DEFORMITY.¹

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THIS article was written to put on record a case in which a complete autopsy was obtainable. For discussion of the etiology, symptomatology, etc., of the condition the reader is referred to Horwitz's article, mentioned below.

DEFINITION. Congenital elevation of the scapula is an affection characterized by an upward displacement of one or both scapulæ, with rotation upon the sagittal or frontal axis. Alterations in shape, size, and density of the bone exist.

HISTORICAL. This condition, both on account of its rarity and because of its puzzling etiology, has been a source of interest for fifty years, the first case recorded being that of Eulenberg's in 1863. In 1891 Sprengel described four cases and advanced a plausible theory to explain the disease; since then the condition has been called "Sprengel's deformity" or "congenital elevation of the scapula." In view of the fact that the high position is not due to elevation but to failure of descent, possibly better terms would be "undescended scapula," "congenital high position," or "scapula alta congenitalis." An analogous instance in terminology is the undescended testicle, which we do not speak of as "congenitally elevated."

FREQUENCY. Up to 1904, 100 cases had been reported. In 1899 Honsell reported the first case of bilateral disease, and up to 1908 14 such cases had been described in the literature. Horwitz,² in 1908, reported 16 cases himself and collected 120 from the literature, bringing the total up to 136. Less than 20 have been characterized by the presence of an associated bony arch, as found in the case we are reporting.

PHYSICAL EXAMINATION. The condition was found by us to exist in a body in the anatomical laboratory of the University of Pennsylvania. The subject was a male negro, about forty years of age, of medium size and good muscular and general development. A notable exception to this general statement was found in the right

¹ Read before the Section on General Medicine of the College of Physicians of Philadelphia, March 23, 1914.

² Amer. Jour. Orthop. Surg., 1908-09. vi, 260.

arm, which was about 3 cm. less in circumference than the left at both the arm and the forearm. In addition to being less developed it could be raised but slightly above the horizontal, this restriction being due to a limitation in movement of the scapula. Surface examination showed that the right scapula was about 6 cm. higher than the left, and between its vertebral border and the spines of the vertebræ a bony lump could be felt.

BONY ANATOMY. The scapula differed from most of the cases hitherto reported in that, with the exception of the scapular index, it was approximately normal in size and showed pronounced roughenings for the attachment of strong muscles. On the vertebral border just below the spine was a triangular facet (Fig. 2), which faced forward and inward and articulated with a bony projection

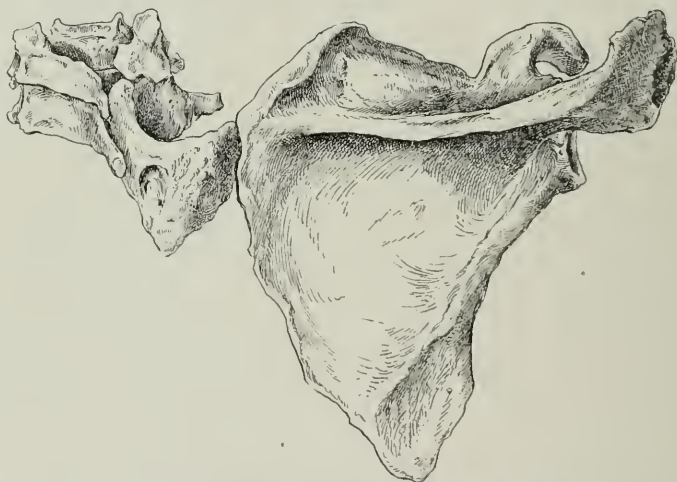


FIG. 1.—Dorsal view of scapula and fifth and sixth cervical vertebræ, showing articulation, exostosis, and spina bifida.

from the sixth cervical vertebra. As is common in Sprengel's disease, the bone had a scroll-like forward curve superiorly (Fig. 3), causing the upper border to project forward as a knife-like edge. The spine made less than a right angle with the vertebræ below it, so that it pointed out and down from the midline of the body instead of out and up, as is usually the case; this latter condition is found normally in the fetus.

THE VERTEBRÆ. The scapula articulated with an exostosis from the sixth cervical vertebra, this growth causing the lump felt on external examination, and the articulation being partly responsible for the restricted upward movement of the arm.

This osseous growth consisted of a strong, markedly curved process of bone (Fig. 1, 2, 3), about 4 cm. in length, which arose from the right lamina of the sixth cervical vertebra. Viewed from the

left it was seen to be roughly triangular, the apex being attached to the lamina and the base being free and directed well toward the right. Both the pedicle and lamina of the right side of this vertebra were much thickened. The growth measured about 2 cm. at the apex and about 5 cm. at the base. Its left side was separated from the vertebral spine by a narrow fissure (Figs. 1, 3), which extended clear to the spinal canal, the latter thus being open posteriorly, while the right side presented a deeply concave groove (Figs. 2, 3), for the accommodation of the semispinalis and rotatores and multifidus spinæ muscles. The upper half of the base had a distinct articular surface, which formed a true joint with the facet upon the mesial border of the scapula. This articulation was of the partially movable type, and was furnished with a capsule, the opening of which allowed the escape of fluid.



FIG. 2.—Ventral view of scapula and sixth cervical vertebra, showing the articular facet on the former and the exostosis on the latter.

A noteworthy point in regard to the vertebræ was that the right laminae of the fifth and seventh, as well as the sixth, cervical vertebræ had not joined those of the left side to complete the arch; a condition of spina bifida (Fig. 1) was present in these three bones. The right lamina of particularly the fifth cervical vertebra was poorly developed, there being a gap (Fig. 1) of $\frac{3}{4}$ cm. posteriorly, which in the articulated state was filled in to some extent by that greatly hypertrophied right lamina of the sixth, from which sprang the osseous growth already described.

MUSCULAR ANATOMY. These anomalies of the skeleton were associated with striking deviation from the normal in the adjacent musculature (Fig. 4), the muscles involved being the trapezius, the levator anguli scapulæ, the rhomboideus major and minor, as well as several anomalous slips.

The trapezius: This muscle was represented by two portions, an upper and a lower, the former being large and very muscular and the latter small, atrophic, and composed mainly of fibrous tissue (Fig. 1). The former was so well developed that it gave the man a square, bull-necked appearance on the right side.

The upper part had the usual origin from the occiput and the cervical spine, while the lower arose from the upper thoracic vertebrae. At the first thoracic vertebra the upper muscular portion



FIG. 3.—View from above of scapula and sixth cervical vertebra.

ended abruptly, and at the point where it crossed the superior angle of the scapula it became densely aponeurotic; here it overlay a bursa. The insertion was normal, with the exceptions that it extended farther medially on the clavicle than usual, and that the insertion into the acromion was thicker and broader than normal, as well as unusually aponeurotic.

The inferior and smaller slip lay below the level of the spine of the scapula. It arose aponeurotically from the vertebral border of the scapula, the vertebral spines and the aponeurosis lying between by means of tendinous fibers, which were interwoven with superficial fibers representing the rhomboids. Under the aponeurotic origin a muscular origin appeared, the fibers intermingling with fibers of the rhomboids, and having a common origin with them from the seventh cervical and first thoracic vertebrae. It inserted into both

lips of the spine of the scapula to within one inch of the acromial tip, thus encroaching upon the origin of the deltoid, and causing that muscle to attach to the spine below the lower lip.

Subtrapezial plexus: Both portions of the trapezius obtained their nerve-supply from the subtrapezial plexus. A notable anomaly of this plexus was that it was composed only of the third and fourth cervical nerves; the spinal accessory failed to pierce the sternocleidomastoid muscle, its fibers terminating within that structure. This condition, while occurring independently of Sprengel's deformity, has been noted by other dissectors of this condition, and may have more significance than has been accredited to it.

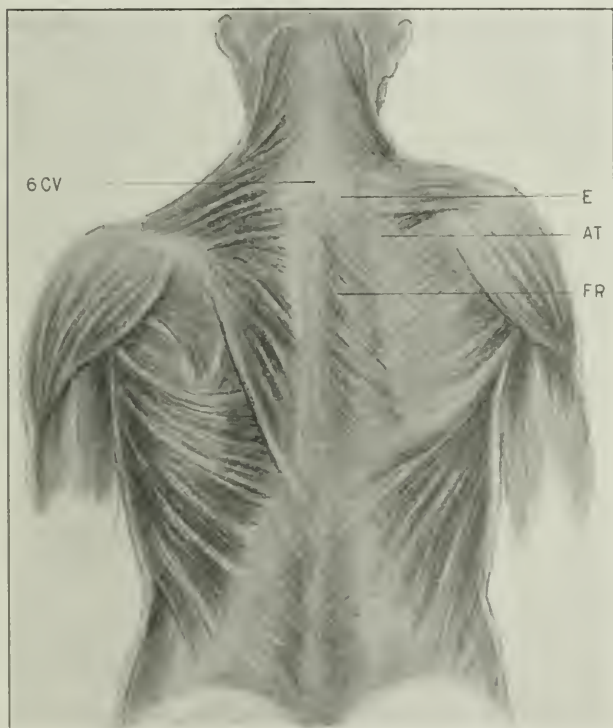


FIG. 4.—Superficial dissection. Shows high position of right shoulder. 6CV, sixth cervical spinous process; E, exostosis; AT, anomalous portion of trapezius; FR, fibrous tissue replacing rhomboid muscles.

The levator anguli scapulæ: This muscle was slightly below normal in size and branched toward its insertion in the form of a Y. One arm of the Y inserted into the superior angle of the scapula and the other into the bony arch. Not over 4 cm. separated the two insertions. If the two arms were spread so as to convert the Y into a T the cross-bar to the T would measure about 5 cm.

The rhomboidei major and minor: These muscles as such were absent, their place being occupied by white connective tissue whose fibers took the same general direction as those of the missing muscles would have done.

The serratus magnus: This muscle was continued upward and inward beyond the vertebral border of the scapula, and interlaced with the rhomboid fibers, making a strong network in which two layers of rather stringy muscle fibers lay.

Upon cutting the scapula away from the trunk two slips from the serratus magnus were encountered, superior to the main muscle and its attachment to the vertebral border of the scapula. One of these inserted into the superior angle of the scapula, and had its origin from the scalenus anticus, medius, and posticus muscles. The other arose from the first rib and the scalenus posticus and inserted into the vertebral border of the scapula.

Anomalous muscles: Immediately posterior to the levator anguli scapulæ was a small slip of muscle which had its origin from the cervical aponeurosis opposite to the fourth cervical vertebra. Its insertion was very close indeed to that of the levator anguli scapulæ and the fibers ran in the same direction, but the two were not continuous. It was supplied by a twig from the fifth cervical nerve, which sent branches into the levator also, so that a fair conclusion would seem to be that it was an accessory levator anguli scapulæ, having its origin from the cervical aponeurosis.

From this description it will be seen that the elevated right scapula could have been movable only to a very slight extent. Most of the muscular attachments would tend to pull the bone upward or at least help to retain it in its high position, and a glance at the scapula or the bony arch will show that there was great muscular strain on these parts.

SOME REMARKS ON THE TREATMENT OF AMEBIC DYSENTERY.

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WITHIN the last two or three years the scientific view-point concerning amebic dysentery and its treatment has undergone a decided change. While there may be present concomitant pathological conditions requiring appropriate attention, it is recognized that the crux of the whole therapeutic problem in this form of dysentery is to destroy the amebæ, and later to heal the ulcerated intestines and cure other complications.

For the destruction of the amebæ the treatment has practically narrowed down to two methods of medication: (1) internal and (2) hypodermic, and in the practice of the writer one method of intestinal irrigation, which is apparently a most useful adjunct. Granted this, the physician may be spared trying the numerous remedies which are recommended, many of which are utterly without merit. These three methods are the internal administration of ipecac, the hypodermic administration of emetin hydrochloride, and the injection into the large intestine of kerosene oil.

INTERNAL ADMINISTRATION OF IPECAC. For many years ipecac has been held in high esteem in East India and the neighboring Oriental countries, and while in some quarters it is unfavorably regarded it has the endorsement of Manson in England, Siler in this country, and others of authority. We have employed it in seven cases, with quite satisfactory results.

In giving large doses of ipecac, several details must be strictly observed or the stomach will not retain it, and consequent failure will ensue.

First of all the drug should be administered only in pill form, and these pills should be coated about a sixteenth or an eighth of an inch with phenyl salicylate (salol), for this coating does not readily dissolve in the stomach before it is absorbed and the violent emetic effect is avoided. The pills should generally contain 5 grains each of the ipecac.

If desired, castor oil may be given ten to twelve hours before the ipecac is to be taken, and a convenient method is as follows: No food is allowed for six hours and no water for three hours. Twenty drops of tincture of opium should be administered thirty minutes before the ipecac pills. The patient should be kept on the back and the pills swallowed with as little fluid as possible. After taking them he should not be allowed to move or speak or expectorate, and the nurse should keep a cold cloth over his throat and frequently bathe his face with cold water. The head should be kept low and both physical and psychic quiet enjoined. After an hour has elapsed he may gently move on his right side to facilitate the passage of the pills through the pylorus, but he should be allowed no water for three hours at least, and then sparingly. By observing these precautions the pills are generally retained; but should they be rejected the same procedure may be repeated the following day or night. After six or seven hours a sufficiency of water is admissible or any light nourishment desired.

The dose of ipecac should be about 40 or 50 grains the first night (eight or ten pills) and reduced 10 grains each night until only 10 grains are given. Following this somewhat rigorous treatment it is well to continue this 10-grain dose every alternate night for ten days to two weeks.

Given this way ipecac appears almost as a specific, and under

its influence the stools become soft and mushy, but soon lose their dysenteric character, and may assume a normal form in a few days. The amebæ generally disappear almost at once, seldom reappearing, though occasionally they do, and then the treatment has to be repeated in its entirety.

HYPODERMIC ADMINISTRATION OF EMETIN. The *modus operandi* of ipecac in its amebicide properties was not well understood until Vedder, in March, 1911, working in Manila, published his findings that a fluidextract of ipecac would kill amebæ in cultures in dilutions as high as 1 to 200,000. The next year Rogers, in Calcutta, found that emetin hydrochloride killed amebæ in stools in dilutions of 1 to 100,000 and began to use this salt hypodermically in cases of amebic dysentery. Since then this preparation has been extensively employed, and favorable reports have come from Asia, Europe, North and South America, and "the isles of the sea."

The dosage recommended by Rogers, and followed by most observers, is from $\frac{1}{3}$ to 1 grain, injected twice a day, daily, or every second day for a week or ten days only.

At present, as contended by Allan, the evidence in regard to the permanence of cure by emetin is extremely meager. In the cases reported by Rogers (32) the active amebæ disappeared promptly after doses of $\frac{1}{3}$ to 1 grain; one case is reported well five months later, and in several of these cases which later came to autopsy from other causes no amebæ were found in sections of the gut. There has been no report on the later history of the remainder of this series of cases, but Rogers thinks they are permanently cured.

Many other apparently permanent cures are reported, including either the amelioration or cure of liver abscesses, but there seems rather a paucity of reports following these cases any considerable length of time. Allan, of Charlotte, reported two cases which promptly cleared up and as promptly relapsed.

Most observers admit that the emetin always kills the active amebæ but not the cysts, the latter being responsible for the relapses. Baermann and Heinemann have detailed in full the treatment of twenty-two cases in Sumatra, furnishing some valuable data. They point out that emetin seems to exert but little effect on cysts and that there is considerable variation in the different preparations of emetin now on the market, as cases which proved refractory to one brand sometimes recovered promptly when emetin from a different manufacturer was employed. One important conclusion at which they have arrived is that while emetin is strongly amebicidal there are certain races of emetin-fast amebæ.

The writer has used this salt in four cases, three of which are still well at one year, eleven months, and ten months respectively. The fourth case suffered a relapse after an apparently normal condition of the bowels for two months, but he fell into other hands, so that details and subsequent symptoms are not available.

At present emetin hydrochloride is the salt mostly used. The size of the dose varies from $\frac{1}{4}$ to 4 grains, and it is also being given by the mouth and rectum—in rare instances intravenously. It is being given daily in single or several doses, on consecutive days, on alternate days, and at irregular intervals. Most observers discontinue it after the clinical symptoms subside or the amebæ disappear from the stools. Allan, a careful and safe clinician, recommends maximum doses—that is, 2 or 3 grains—instead of small doses. As no one has reported bad results except a transient nausea, and as small doses do not satisfactorily eradicate the amebæ, the conclusion of Allan seems sound and practicable.

The employment of emetin should be reinforced by rest in bed, appropriate diet, and other measures indicated for ulcerated intestines, perhaps abscessed liver, and a depleted body. As yet we do not know the best method as to dosage, frequency, or duration of treatment in the administration of emetin, but the mass of clinical reports now being poured into our literature will soon definitely settle these questions.

INJECTION OF KEROSENE OIL. This procedure is of recent date and has not come into general use, but is a valuable aid in the management of amebic dysentery. For an adult about 1 pint of pure oil should be employed, and with the patient in the knee-chest position, it should be injected into the bowel with a colon tube. He should keep this position, in an exaggerated manner if possible, for several minutes so that the oil will gravitate well into the colon. This should be retained for thirty or forty minutes and then be permitted to escape, though if all is not at once evacuated no alarm need be felt. R. T. Dorsey reports one case where, through a misunderstanding of orders, the oil was allowed to remain in the bowel over two hours. No ill effects occurred. We have not in any instance depended upon the oil alone in amebic dysentery, but in the stubborn diarrhea accompanying pellagra we have in a number of instances noted marked improvement following this procedure alone after various astringents had failed to afford relief.

This injection may be repeated daily for three or four days, and then occasionally as required. It will be found, however, that not many will be needed, for unless the case is extremely far advanced improvement will promptly set in.

Amebic dysentery, like duodenal ulcer, is probably much more prevalent than has been supposed, and its frequency has been shown by more thorough diagnostic methods. The only way a positive diagnosis of amebiasis can be made is by the microscope, and the finding of the protozoa in the stools. In regions where the disease is endemic and a microscope is not available one can reasonably infer its presence by the most prominent symptoms, namely, abdominal soreness, which is increased on pressure and

extends along the course of the colon, especially when there is maximum intensity over the cecum and ascending colon. I believe with Musgrave, that the presence in the stools of any form of ameba in warm or tropical regions should be considered diagnostic for purposes of treatment, whether or not active symptoms are present.

Thus by carefully examining every suspected case of possible amebic infection and by early and energetic treatment along the lines herein considered this otherwise serious disease can in nearly every instance be promptly and permanently relieved.

THE DIAGNOSIS OF TUBERCULOSIS IN EARLY LIFE.¹

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THIS paper has to do with the chronic form of pulmonary tuberculosis in children, and does not consider the acute manifestation of the disease, such as general miliary tuberculosis, tuberculous meningitis, or the acute bronchopneumonic form which complicates or follows some one of the acute infectious diseases; nor does it consider the surgical aspects of the disease. There are two reasons for this: In the first place, children suffering from the disease in any of the forms above mentioned usually are taken to the general hospitals and are rarely seen in a dispensary devoted exclusively to tuberculous patients, and in the second place, while individual cases may present difficulties in making a diagnosis, the clinical picture in the majority of cases of this type is usually readily recognized.

Excluding the types just mentioned the recognition of tuberculosis in children is either extremely easy or most difficult, the determination of a positive or negative finding depending almost entirely on the attitude of the particular observer. Thus, in some instances, all children having a tuberculous parent have been considered as being likewise tuberculous. In others the occurrence of a positive tuberculin reaction or the presence of palpable lymph nodes in the neck have been considered as sufficient evidence to designate the child as having tuberculosis.

¹ Read before the Philadelphia Pediatric Society, May 12, 1914.

The reason for the current belief that tuberculosis is an extremely common finding in children, particularly in children of the poorer classes, is largely due to the general acceptance of the theory that infection with tuberculosis is commonly acquired in childhood. That this is true in many, possibly the majority, of cases everyone agrees. That it is invariably the case, however, has not been proved. The theory that infection in childhood is the universal one, if it could be shown conclusively to be true, would at once dispel all the uncertainties regarding the etiology of the disease; and furthermore, it would change very radically our procedures in the way of prevention.

At first sight the etiology of tuberculosis seems perfectly clear. If, however, we analyze the subject more closely we are forced to admit that we know very little about it. This may seem to be putting the question too strongly; but let us examine some of the facts and see how matters stand. That infection with the tubercle bacillus is widespread, and, furthermore, that it commonly occurs early in life, is practically universally acknowledged. So far we stand on reasonably firm ground. When, however, we attempt to explain why relatively few of those thus infected develop tuberculosis which is clinically recognizable while the majority of infected individuals pass through life with no manifestations of the disease we can only hazard a surmise.

A number of factors must be considered—namely, the question of hereditary predisposition, the influence of race, poor food, bad housing conditions, overwork, mental worry, acute illness, dissipation, and, lastly, reinfection later in life. Anyone of these may be sufficient to lower the resistance of the individual to a point where the natural defences of the body can no longer keep in check the multiplication and spread of tubercle bacilli already within the body. It seems apparent, therefore, that while many children may receive an implantation early in life the determining factor as to whether they become openly tuberculous later in life is dependent on a number of factors, most of which have to do with unsanitary evils. For the most part the problem becomes one of a diagnosis of the social surroundings of the child rather than of its physical condition. It is, of course, understood that the same effort should be made with children as with adults to recognize those having true clinical tuberculosis.

The present study relates to 362 children examined at the Phipps Institute between three and four years ago. The majority of them were brought for examination because of tuberculosis in one or the other parent and not because the children themselves had any symptoms. Reports as to the condition of 111 of these children have been obtained within the past two or three months. The examination of these children was made by five men on the dispensary staff and a study of the records affords a good illustration

of the points of view of different observers. Of the 362 a positive diagnosis of tuberculosis was made in 96 (26.5 per cent.). In studying the records the conviction cannot be escaped that this percentage is either too low or too high for the reason that many cases designated as non-tuberculous could readily be classed as having tuberculosis, and *vice versa*. In other words, undoubted evidence of tuberculosis was present in but a few; in the remainder the individual's point of view seemed to be the determining factor in making a positive or negative diagnosis. It might be well to mention at this point that of the 111 of these children recently heard from, 25 had a diagnosis of tuberculosis over three years ago. All of these children are reported as well except 2, 1 of whom recently died of tuberculosis and 1 of a cause unknown.

SYMPTOMS. The symptomatology of tuberculosis in adults, while subject to many vagaries, is invaluable in making a diagnosis. Indeed in many cases of incipient tuberculosis it is our chief reliance in determining the nature of the trouble. In children, on the other hand, we are deprived of much of the value of symptoms, because of the inability of young children to give a correct description of their trouble; and in the case of the present group the difficulty is augmented by reason of the fact that they are for the most part, the children of foreign parents, who, in many instances, are almost as useless as the children themselves so far as giving a history of the illness is concerned.

TEMPERATURE. One of the most reliable means of detecting early tuberculosis in the adult is the slight rise in temperature which may occur daily or only every few days. In children, however, little reliance can be placed in these slight elevations of temperature, for the reason that growing children normally have a higher temperature than adults. Landois² gives as the normal limits 99.5° to 100.1° F. (37.87° to 37.62° C.) in children from five to nine years; 190 of the 362 children had a temperature of from 99° to 100° F. The reason for this is, in all probability, a more active metabolism, although other influences of undetermined origin may also, in part, be contributory; 143 (31.3 per cent.) complained of cough. As a rule this was of but a few days' duration; 223 (61.6 per cent.) stated that there was no expectoration. The sputum of 37 was examined, with negative results. Hemoptysis was said to have occurred in 16. Chest pain was complained of in 95. Hoarseness of a transient character was noted in 48 and persistent hoarseness in 9. Night sweats occurred in 52.

Cough, if it has persisted for weeks, hemoptysis, and persistent hoarseness would have the same significance in the child as they do in the adult.

PHYSICAL SIGNS. In taking up the question of physical signs in the chests of infants and young children we have to consider

² Text-book of Human Physiology, 10th ed., p. 391.

what is probably the most difficult phase in the art of physical diagnosis. And while it is true that the underlying principles which enable us to detect disease in the chest are the same, whether it be adult or child, there are certain differences between the two which must be kept in mind. Generally speaking the man whose training has been confined to the examination of adults alone, or children alone, is likely to draw false conclusions when he invades one or the other field, and much that has been written regarding the presence of chronic tuberculous lesions in the lungs of children has been contributed by those whose standards have been obtained by the examination of adults with tuberculosis.

Furthermore, it must be borne in mind that the clinical forms of human tuberculosis in different ages possess correspondingly different anatomical features, a knowledge of which is necessary for the understanding of the interpretation of physical signs. In the majority of instances, tuberculosis, when it involves the lungs of infants and young children, is bilateral, widespread (either of the miliary or bronchopneumonic form), and acute in character.

In the adult, on the other hand, the disease begins at one or the other apex, follows a fairly definite course in its progress, and is chronic in character, although subject to periods of acute activity. As a rule the clinical manifestations of tuberculosis as they occur in infants and young children differ from the adult type, and this is not altered by the fact that the juvenile type may occur in adults, and *vice versa*.

It is not altogether easy to fix definitely the age period at which the signs peculiar to children cease. Some have arbitrarily fixed this limit at the age of six years, although in our judgment ten years would be more nearly correct.

Probably the most distinctive difference between the adult and the child is that in the latter all of the sounds are exaggerated. Not only is the breathing of the familiar puerile type, but all the vocal sounds are increased, and in addition the percussion note is commonly hyperresonant.

As an illustration of how the exaggeration of physiologically normal signs may be misinterpreted in the child it is interesting to note that of 79 children in this group who were charted as having abnormal physical signs no less than 67 had impairment and bronchovesicular breathing at the right apex. It will be recalled that in the adult the right apex normally has a slightly impaired note, prolonged expiration, and increased fremitus, and that the explanation of this was pointed out by Fetterolf³ as being due to close proximity of the trachea to the right upper lobe. The very high proportion of cases in this group, with apparent disease at the

³ Archives of Internal Medicine.

right apex, would seem to indicate that what was in reality a normal finding was interpreted as being pathological.

One's belief in this is strengthened from the result of reports on 111 of these children three or four years after the first observation. Of these 111 cases 17 were noted as having a diseased right apex, and in 2 more both apices were supposed to be affected. At the present time 17 of the 19 are noted as being in good health, 1 has died of tuberculosis, and 1 still has some cough.

In addition to the exaggeration of the breath sounds already noted the respiratory sounds in children are subject to a number of vagaries, and the younger the child the more difficult is the interpretation of the auscultatory signs.

The expired air may, for instance, be directed into the pharyngeal vault or against the roof of the mouth, with the result that a bronchial quality of breathing is heard all over the chest. This can be obviated if the child is old enough to learn how to breathe properly. Then again in young children and infants the lungs at times seem to move independently of one another, with the result that loud puerile breathing is heard over one side, while over the opposite side the breath sounds are almost inaudible, and this condition shifts from side to side. This peculiarity is often due to faulty posture. If care is not taken to see that the child sits straight, and that one or the other side is not held tense, not only will there be very faint or nearly absent breath sounds on the cramped side, but in addition the percussion note may be impaired, or indeed absolutely dull. We have often demonstrated this fact to students and shown them how the signs on the two sides can be almost instantly reversed. This fact is worth remembering, as the unwary may make a diagnosis of pneumonia or pleural effusion.

In adults one of the most valuable means of detecting early pathological changes at the apex is the restriction of expansion over the affected area. In children this procedure is almost useless, except in a few of the older ones, because of jerky movements, and what has seemed to us to be often the case, the fact that the lungs of infants and young children do not seem to possess the same synchronous movement that the adult organs possess.

LYMPH NODES. In nearly every article dealing with the diagnosis of tuberculosis in children great stress has been laid on the presence of palpably enlarged cervical lymph nodes. Indeed in not a few instances, in which surveys of large groups of children have been made, this apparently has been the only evidence on which the diagnosis was made. The fact has been ignored that the age of childhood is likewise known as the lymphoid age, and that all children, irrespective of their social condition, have lymph nodes which are readily palpable. The enlargement of the lymph nodes is not readily detected until about the second year, but

from then on until shortly before or after the age of puberty this is the case, although as the child approaches adolescence certain groups, such as the epitrochlear, the axillary, and the inguinal, tend to shrink in size and become less easily detected. The submaxillary node at the angle of the jaw is usually the largest under normal conditions, and is usually the last to shrink to a size that it can no longer be palpated.

In our experience all of the superficial lymph nodes can be palpated readily in the majority of cases if the children are systematically examined from this standpoint.

To confine the examination to one group, such as the cervical and because the nodes in this situation are palpable, to assume that it is an evidence of tuberculous infection does not seem in any way justifiable, especially so in view of the fact that all the lymph nodes of the body are hypertrophied according to adult standards.

If there exist in the neck a single large node or a tumor mass made up of a number of nodes, which are matted together and adherent to the surrounding tissues, the presumption is strong that we have to deal with a tuberculous adenitis, and especially so if there is evidence of softening, or the overlying skin is inflamed. This, however, is true scrofula, and has nothing to do with nodes which vary in size from that of a bean to a split pea, or smaller, which are freely movable, and which manifest neither softening nor inflammation.

Of the 362 children here reported the records show the following results: cervical, 250; submaxillary, 202; axillary, 209; epitrochlear, 94; inguinal, 212.

It is to be borne in mind that the above records are of positive value almost entirely, and that the discrepancies between the different groups are largely because the examination was not complete.

Still another group of lymph nodes must be considered, namely, the bronchial. Of recent years a great deal has been written on the physical signs and symptoms of tuberculous enlargement of this group, especially the former. Some writers have reported quite a high percentage of cases in which this condition existed. Much of the evidence on which such a diagnosis is made seems open to question, especially from the standpoint of physical signs. In our opinion the alleged percussion changes, such as the semilunar areas in the second and third interspaces anteriorly and the vertebral dulness posteriorly, which are supposed to be indicative of such enlargement, are fanciful rather than real, and the questionableness of such findings has been shown by Gittings and Fetterolf⁴ in their work on frozen sections of the thoraces of infants and young children.

⁴ Some Anatomical Features of the Child's Thorax; Their Application in Physical Diagnosis, *Amer. Jour. Dis. of Children*, 1911, vol. i.

X-ray studies made by Pancoast of children in whom we suspected this condition might exist have given negative results in the majority of instances. The mere fact that these nodes may show some enlargement on x-ray examination is no proof that they are pathologically enlarged in view of the fact that we know all the superficial nodes are hypertrophied normally.

The truth of the matter is that this diagnosis is not easy. Children below par and who have a persistent hard, brassy cough, usually unproductive, seem to be the ones most likely to suffer from this condition.

In this connection it may not be amiss to say something regarding the tonsils, as they are regarded by many as portals of entry for the tubercle bacillus. Here again we are dealing with lymphoid tissue, which in children is excessive, and which, as the years pass, tends to shrink until the relatively large tonsil of the child is transposed to the atrophied one of old age. The removal of tonsils which are enormously enlarged, and which are associated with frequent colds, or inflammation of the tonsils themselves, is one thing, but the wholesale massacre of these organs simply because they are enlarged, according to adult standards, is in our opinion a mistake. Our records show that of 290 children examined from this standpoint 110 were noted as having some enlargement of the tonsils.

Mouth-breathing was noted in 144, although adenoids were detected in but 24. These latter figures are not trustworthy, however, as but a small percentage had a skilled nose and throat examination.

TEETH. While the condition of the teeth has no direct bearing on the diagnosis of tuberculosis in growing children it is coming to be recognized more and more that the general health of the child may be adversely affected by a large number of badly decayed teeth. Thus bad teeth may be one of the contributing factors in lowering the general resistance and permitting the latent tuberculous infection to gain the upper hand.

Of the 191 children examined as to the condition of their teeth, 48 were classed as good, 69 as fair (that is but two or three decayed teeth), and 74 as being very bad.

TUBERCULIN TESTS. The accepted belief at the present time is that a positive reaction to one of the tuberculin tests is indicative of a tuberculous lesion somewhere within the body. A positive test does not mean, however, that the individual has clinical tuberculosis. It must clearly be kept in mind that there is a great difference between tuberculosis that is clinically recognizable and hypersensitiveness to tuberculin. Hypersensitiveness is extremely common, and is encountered in a large proportion of children, the frequency with which it is met increasing rapidly from the second to the fifteenth year. It is a great mistake to assume that because

a child reacts to some one of the tuberculin tests that it is tuberculous in the sense that it needs active treatment; and, as we shall later point out, a negative tuberculin test does not entirely free us from responsibility.

In regard to the tests themselves there are certain facts which should be kept in mind. First as regards the subcutaneous test. This is rarely employed in children, especially the very young ones. At one time the test was extensively used in adults and a positive reaction was, and by many still is, regarded as conclusive proof that the individual has tuberculosis. Of recent years, however, some observers have warned against its use, pointing out that the test is capable, in certain instances, of stirring an inactive lesion into an active one. Furthermore, there is now a tendency not only to limit the use of the test, but in addition to ignore the constitutional symptoms of a reaction (such as fever, joint pains, local reaction, etc.) and to call positive only those cases which give a focal reaction, such as rales at a suspected apex, or some pain, redness, and swelling in a suspected joint.

The cutaneous or von Pirquet test has achieved enormous popularity by reason of its simplicity, and also because it is widely credited with being positive evidence of tuberculosis. In children under two years of age it is valuable evidence when positive and usually means clinical tuberculosis. Beyond the second year, however, it loses much of its positive value, and the older the child the more unreliable it is as an evidence of true tuberculosis.

The percutaneous or so-called Morro test has about the same significance.

Finally we have to consider the conjunctival test introduced by Wolf-Eisner and Calmette. The majority of observers have come to regard this test as dangerous, because of the possibility of producing an inflammatory condition which may lead to serious damage of the eye. According to Hamman and Wolman,⁵ who have employed the test in a large series of cases, the test is free from danger, and is superior to the Morro and von Pirquet tests in that it is not so sensitive and that a positive reaction points strongly to an active rather than a latent process, especially so when supported by other indications.

Of the 361 children under discussion, 100 gave a positive and 93 a negative von Pirquet reaction. This does not represent the total number given the test, as many more received it but did not return to the dispensary to see whether the reaction was positive or negative.

The question naturally arises, What is the practical value of the von Pirquet or Morro test in determining the children who have true tuberculosis and those who can be disregarded? We are

⁵ Tuberculin in Diagnosis and Treatment, 1912.

forced to conclude that they are of little value except as an evidence of hypersensitiveness. We have repeatedly seen anemic, undernourished children with or without tuberculous parents who gave no reaction; and, on the other hand, we have encountered children who presented no physical signs who were in robust health and who had violent skin reactions.

SOCIOLOGICAL CONDITIONS. The really important thing to determine in regard to these children is this: Are they physiologically normal, and if they show any evidence of being below par, what is the cause? In the great majority of instances it will be found that those below the normal are suffering from sociological evils rather than tuberculosis. Viewed in this light it is relatively unimportant whether the child shows evidences of hypersensitiveness or not, because if allowed to remain amid unsanitary surroundings it will quite likely become infected, or if infection has already occurred the chances of true clinical tuberculosis developing are greatly enhanced.

It has been recognized for some years that the tuberculosis problem is a complex one and one that is not to be solved by purely medical procedures, so that in determining the question as to whether a child is in need of preventive treatment we are in the majority of cases confronted with a condition of malnutrition, partly the result of poor and insufficient food and partly the result of unsanitary living conditions. In other words, we have not discharged our duty to the child by simply saying that he has or has not tuberculosis.

Thus the general appearance of 141 of the 362 children was noted as being bad, while of 155 whose weight was recorded, 82, or 52.9 per cent., were found to be under weight for their age.

The term "pretuberculous" has been applied to that large group of children who, while not clinically tuberculous, are objects of suspicion, either because of tuberculous parentage, poor living conditions, or who are themselves badly undernourished. The term "pretuberculous" has been objected to, but as it has come to be so generally understood that it means children who, if allowed to drift, are prone to become actively tuberculous, that we can see no great reason for not using it.

Certain interesting facts are revealed as to the social conditions of the 362 children forming the basis of this paper, and while none of the facts are new, they will bear repeated emphasis.

These 362 children belonged to 210 families. What constitutes a proper income for a family of three or five or seven is somewhat conjectural, depending as it so often does on habits of thrift or extravagance. It is usually assumed, however, that not more than one-quarter of the income should be expended for rent, and that the food allowance should be \$1.50 per week per capita, approximating 21 cents per capita each day. Of 154 families studied on

this basis the number with an adequate income was 68, or 44.17 per cent., while 86, or 55.83 per cent., had an inadequate income; 50 families were paying an excessive rent.

The following table shows the extent to which over-crowding exists:

Families living in 1 room to each member	102
" " 1 " 2 members	70
" " 1 " 3 "	25
" " 1 " 4 "	8
" " 1 " 5 "	2
" " 1 " 6 "	2
" " 1 " 7 "	1
Total	210

Distinct overcrowding occurred in 38, or 18 per cent., of the 210 families.

Still another aspect of the problem is seen in the following table, which shows the number of rooms occupied by each family:

Families living in 1 room	17
" " 2 rooms	39
" " 3 "	52
" " 4 "	42
" " 5 "	20
" " 6 "	29
" " 7 "	4
" " 8 "	4
" " 11 "	1
" " 13 "	1
" " 14 "	1
Total	210

No data is available as to the hygienic conditions of these families at the time of the original examination, but we do know the conditions under which 111 of the children are at present living. A recent investigation shows that 48, or 46.2 per cent., of the children are living in poor, dirty, and unhygienic surroundings, while 13, or 11.7 per cent., of the home conditions are classed as only fair. The remaining 50 are living in clean surroundings.

Two facts are now well known: (1) that both the morbidity and mortality rates are always higher among those living under unsanitary conditions; and (2) that there is almost instant improvement in children when they are given sufficient nourishing food and healthful surroundings. The latter fact is now well established by reason of the results obtained in open-air schools and in sanatoria which admit children of the so-called pretuberculous type.

We would, therefore, repeat that the main problem consists in determining whether the child is physiologically normal, and if not, of using every endeavor to provide the means of making it so.

THE DIFFERENCE IN THE MORPHOLOGY OF BLOOD IN GASTRIC ULCER, DUODENAL ULCER, AND IN CHRONIC APPENDICITIS, BASED UPON FIFTY OPERATIVELY DEMONSTRATED CASES.¹

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It is unnecessary to enter into a discussion of the difficulty, in a large number of cases, of differentiating between gastric and duodenal ulcer and between these and chronic appendicitis, for the reason that their symptoms and signs are frequently alike.

The object of this paper is to show that correct interpretations of blood-findings in these pathological affections may be of great aid to the clinician for the differential diagnosis, and especially in cases where all hitherto known methods of examinations, including x-rays, fail to clear up the situation. In other words, it is our intention to show that there is a difference in the blood-picture between gastric ulcer, duodenal ulcer, and appendicitis.

While partial attention has been paid to the blood in appendicitis, this cannot be said about the blood in ulcers of the stomach and duodenum. To the frequency of polycythemia in non-hemorrhagic duodenal ulcer reference was made in three previously published papers.² Our hematological studies convinced us, too, that the morphology of the blood differs in gastric ulcer with the site of the lesion in the viscus. In patients with pyloric ulcers the blood-picture varies from that of non-pyloric ulcers.

MATERIAL. Our studies are based upon a large material, but as cases without operative evidence may be open to criticism, we shall refer only to fifty operatively demonstrated cases.

The material, which was drawn from the Vanderbilt Clinic and from our private practice, consists of 12 gastric ulcers in ten males and in two females, 18 duodenal ulcers in fifteen males and in three females, and 20 cases of appendicitis in ten males and in ten females.

For the reports of operative findings I am indebted to the following surgeons: Dr. Charles Peck, 17 cases (3 gastric ulcers, 4 duodenal ulcers, and 10 cases of appendicitis); Dr. G. E. Brewer, 3

¹ Read before the Section of Medicine, New York Academy of Medicine, April 21, 1914.

² Friedman, G. A., A Hitherto Undescribed Form of Polycythemia and its Possible Relation to Duodenal Ulcer, Chronic Pancreatitis, and a Disturbance of Internal Secretions (Epinephrin), *Medical Record*, October 18, 1913; Weitere Erfahrungen über Polyzythämie beim chronischen uncomplicierten Duodenalgeschwür, *Arch. f. Verdauungskrankheiten*, Band xix, Ergänzungsheft, 1913; The Value of Polycythemia for the Diagnosis of Duodenal Ulcer, Based upon Sixteen Operatively Demonstrated Cases, *Medical Record*, May, 1913.

cases (1 gastric ulcer and 2 appendicitis); Dr. Charles Dowd (1 duodenal ulcer); Dr. A. A. Berg, 18 cases (5 gastric ulcers, 8 duodenal ulcers, and 5 appendicitis); Dr. A. G. Gerster, 5 cases (2 gastric ulcers, 2 duodenal ulcers, and 1 appendicitis); Dr. W. Linder, 2 cases (1 gastric and 1 duodenal ulcer); Dr. F. Kamerer, 1 case (appendicitis); Dr. G. D. Stewart, 1 (duodenal); Dr. Charles Goodman, 1 (duodenal); Dr. M. Bookman, 1 case (appendicitis).

TABLE I.—Gastric Ulcer. Operative Findings.

1. Double ulcer (indurated) at lesser curvature, anteriorly and posteriorly proximal to cardia.
2. Callous ulcer of the size of a quarter (United States currency) at lesser curvature, very near to cardia.
3. Callous ulcer (posterior wall near cardia).
4. Indurated ulcer at lesser curvature about two inches from pylorus.
5. Indurated ulcer at pylorus.
6. Indurated ulcer near pylorus.
7. Ulcer at anterior surface of pylorus.
8. Callous ulcer at pylorus.
9. Indurated ulcer at pylorus.
10. Double ulcer at pylorus and lesser curvature near cardia.
11. Ulcer near pylorus posteriorly.
12. Pyloric ulcer and obstruction.

TABLE II.—Gastric Ulcer. Blood.

Number.	Hemoglobin, per cent.	Red-blood cells.	White-blood cells.	Polynuclears.	Small lymphocytes.	Small mononuclears.	Large lymphocytes.	Large mononuclears.	Eosinophiles.	Basophiles.	Transitionals.
1	60	5,800,000	16,120	86.0	13.0	0.0	0.0	0	0.0	0.0	1.0
2	110	6,030,000	11,200	63.5	30.0	2.0	1.5	0	1.5	0.0	1.0
3	89	5,200,000	13,400	69.0	20.5	1.5	3.5	0	2.5	0.0	3.0
4	83	5,780,000	10,600	75.0	15.5	2.0	2.5	0	0.5	0.0	3.5
5	70	3,900,000	4,800	46.0	30.0	17.0	3.0	0	4.0	0.0	0.0
6	55	3,400,000	4,840	44.0	36.0	15.0	0.0	0	4.5	0.5	0.0
7	65	5,380,000	5,600	71.0	15.0	10.0	0.0	0	4.0	0.0	0.0
8	65	4,520,000	9,800	52.0	31.0	12.0	0.0	0	3.5	0.0	0.1
9	72	4,360,000	4,100	48.0	13.0	16.0	2.0	0	4.0	0.0	0.0
10	85	4,390,000	12,600	60.0	25.0	0.0	0.5	0	3.5	0.5	0.5
11	70	4,300,000	6,800	55.0	30.0	8.0	2.0	0	4.0	1.0	0.0
12	65	5,459,000	9,800	75.0	14.0	8.0	1.5	0	0.5	0.0	1.0

Table I indicates that in 10 cases the ulcers were single and in 2 double (Cases 1 and 10). In Cases 2, 3, and 4 (single ulcers) and in Case 1 (double) the site of the lesion was at the lesser curvature proximal to the cardia. One of the ulcers in Case 10 was found at the same region of the lesser curvature, and the second ulcer at the pylorus. In 5 cases (5, 7, 8, 9, and 12) the site of the ulcers was at the pylorus, without causing obstruction except in Case 12. In Cases 3 and 11 the ulcers were found to be prepyloric or parapyloric.

In order to avoid repetitions the gastric ulcer cases are divided into two groups: (1) non-pyloric, where the lesion was at lesser curvature, nearer the cardiac orifice, and (2) pyloric group, where the lesion was at the pylorus or very near to the pylorus (parapyloric or prepyloric)

Case 10, with ulcers at the pylorus and lesser curvature, nearer to the cardia belongs to both groups.

The average percentage of hemoglobin was for the non-pyloric group	85
The average percentage of hemoglobin was for the pyloric group	65
Average	75
The average number of red-blood corpuscles was for non-pyloric	5,700,000
The average number of red-blood corpuscles was for pyloric	4,463,000
Average	5,081,000

The somewhat higher counts of red-blood corpuscles in Cases 7 and 12 in the pyloric group were probably due to concentration of blood, as frequent vomiting is noted in the histories of these cases.

White-blood Corpuscles. Mild leukocytosis was present in the four cases of the non-pyloric group and in the case which belonged to both groups. There was no leukocytosis in the pyloric group, but frequently leukopenia.

Lymphocytes. A relative lymphocytosis was frequently found in the pyloric group, but no lymphocytosis in the non-pyloric.

Small mononuclears were markedly increased in the pyloric group, showing no increase in the non-pyloric.

A marked increase in large lymphocytes was not noted in either of the two groups.

Large mononuclears were absent from the blood in the two groups.

A relative increase in eosinophiles (4 per cent. and 3.5 per cent. was present in the pyloric group with the exception of Case 12 (pyloric obstruction). There was no relative eosinophilia in the non-pyloric group.

An increase in transitionals was noted in 2 cases of the non-pyloric group, but no increase in the pyloric group.

CHARACTERISTICS OF THE TWO GROUPS.

Pyloric group.	Non-pyloric group.
Anemia.	Polyglobulia.
Absence of leukocytosis.	Leukocytosis.
Relative lymphocytosis.	Absence of relative lymphocytosis.
Increased small mononuclears.	No increase in small mononuclears.
Relative eosinophilia.	Absence of relative eosinophilia.
No increase in transitionals.	Occasional increase in transitionals.

CHIEF CHARACTERISTICS.

Pyloric group.	Non-pyloric group.
Anemia.	Polyglobulia.
Absence of leukocytosis.	Leukocytosis.
Relative eosinophilia.	Absence of relative eosinophilia.

REMARKS. The determinations of the percentage of hemoglobin were made with the Sahli hemoglobinometer. The complete blood-examinations were made while the patients were on fasting stomach (early in the morning). The smears for differential counts were stained with Jenner's stain. As a rule not less than 200 white-blood corpuscles were counted. A differentiation was always made between small mononuclears and small lymphocytes. As small mononuclears were counted such of the small lymphocytes which showed a distinct nucleus, otherwise they were counted as small lymphocytes. There was also made a distinction between large lymphocytes and large mononuclears. The examinations of the blood in the cases of gastric ulcer, as in the following cases of duodenal ulcer and chronic appendicitis, were made repeatedly.

TABLE III.—Duodenal Ulcer. Operative Findings.

1. Broad scar.
2. Double ulcer; gastric and duodenal.
3. Ulcer at posterior wall and two gall-stones.
4. Ulcer at anterior wall.
5. Ulcer at posterior wall.
6. Scar at first portion and gall-stones.
7. Broad adhesions between first portion and gall-bladder. No stones.
8. Broad scar and adhesions.
9. Soft ulcer.
10. Perforated ulcer.
11. Soft ulcer at first portion and esophageal carcinoma adherent to aorta.
12. Broad adhesions between first portion and gall-bladder. No stones.
13. Scar and soft ulcer at first portion.
14. Ulcer at anterior wall.
15. Broad scar.
16. Ulcer at anterior wall.
17. Ulcer at anterior wall, chronic appendicitis, and gall-stones.
18. Ulcer at posterior wall and chronic appendicitis.

TABLE IV.—Duodenal Ulcer. Blood.

Number.	Hemoglobin, per cent.	Red-blood cells.	White-blood cells.	Polynuclears.	Small lymphocytes.	Small mononuclears.	Large lymphocytes.	Large mononuclears.	Eosinophiles.	Basophiles.	Transitionals.
1	95	6,700,000	8,740	57.0	41.0	1.0	0.0	0.0	0.0	0.0	1.0
2	90	6,576,000	14,960	63.0	33.0	0.0	2.0	0.0	2.0	0.0	0.0
3	82	5,660,000	7,600	64.4	25.5	0.0	3.27	0.0	1.4	0.0	4.6
4	112	6,510,000	9,000	69.0	22.5	4.5	0.0	0.0	3.0	0.5	0.5
5	100	5,730,000	8,800	65.5	17.5	10.0	0.0	0.0	1.5	1.0	4.5
6	80	5,580,000	9,100	54.0	33.0	1.0	7.0	0.0	0.5	0.5	4.0
7	90	6,000,000	8,920	65.0	30.5	1.5	0.0	0.0	0.5	0.5	2.0
8	85	4,300,000	4,500	52.0	35.0	7.0	1.0	0.0	4.0	0.5	0.5
9	65	4,473,000	7,600	73.0	17.0	7.0	1.0	0.0	3.0	0.0	0.0
10	94	5,130,000	21,000	75.0	16.0	2.5	0.0	0.0	2.0	0.0	2.0
11	86	5,800,000	6,000								
12	96	5,600,000	5,600	64.0	31.0	0.0	0.0	0.0	1.0	0.0	4.0
13	100	6,400,000	8,060	60.0	30.0	2.0	2.0	0.0	1.0	0.0	5.0
14	120	5,700,000	8,060	61.0	38.0	0.0	0.0	0.0	0.5	0.5	0.0
15	70	6,630,000	9,940								
16	90	7,610,000	9,800	58.0	37.0	0.0	1.5	0.0	1.0	1.0	1.5
17	100	6,720,000	9,200	55.0	26.0	8.5	1.0	2.0	5.0	0.5	2.0
18	100	6,060,000	8,200	71.5	14.0	4.0	4.0	1.0	1.5	0.5	3.5

Table III indicates that the lesions were all at the first portion of the duodenum. In 8 cases callous or indurated ulcers were found, in 4 scars, in 2 soft ulcers, in 1 soft ulcer and scar, in 1 perforated ulcer, in 2 broad adhesions between the duodenum and the gall-bladder, without stones in the latter.

In Case 2 double ulcer was found (duodenal and gastric near the cardiac orifice). This case therefore belongs to the duodenal and non-pyloric groups. In Cases 3, 6, and 17 gall-stones were likewise found. In Cases 17 and 18 chronic appendicitis, which also was present, necessitated appendectomy. Case 9 was the only one of bleeding ulcer. Case 11 came to operation originally for carcinoma of the esophagus. In exploration of the viscera a soft ulcer at the duodenum was detected, which did not give a single symptom or sign pointing to the condition found. In all the cases with the exception of Cases 6 and 11, gastro-enterostomy was done.

Table IV indicates that the average percentage of hemoglobin for duodenal ulcer was 90. The average number of red-blood corpuscles was 6,000,000. Polycythemia was found in 15 cases out of 18, or in 83 per cent.

There was no leukocytosis present except in the case, which also belonged to the non-pyloric group and in the case of perforated ulcer. Occasionally leukopenia was present.

There was no relative lymphocytosis.

An increase in small mononuclears was rarely noted.

Relative eosinophilia (4 per cent. and over) was marked only in 2 cases; in Cases 8 and 17 (duodenal ulcer and appendicitis).

Large mononuclears were absent in all the cases of duodenal ulcer except in the two in which appendicitis was likewise found. An increase in transitionals was noted frequently.

REMARKS. The blood of the patients who remained under observation after gastro-enterostomy was examined in shorter or longer intervals after operation. The blood-picture remained the same with reference to polycythemia and other findings.

Characteristics for non-hemorrhagic duodenal ulcer are: Polycythemia; absence of relative lymphocytosis; absence of relative eosinophilia. Chief characteristic: polycythemia.

As histories of patients with examinations of feces were given elsewhere, here it should only be mentioned that the presence of occult blood in the stools is not as frequent as it is generally believed. A history of repeated intestinal hemorrhages was given in Case 9, in which the blood showed anemia.

From 17 cases of non-bleeding ulcers in only 2 polycythemia was absent; the value of the latter for the diagnosis of non-bleeding duodenal ulcer is very evident.

TABLE V.—Appendicitis. Operative Findings.

1. Fibrinous appendicitis.	11. Congested appendix and bands around.
2. Chronic and adhesions.	12. Chronic appendicitis with concretions.
3.	13. Chronic.
4. Adherent appendix.	14.
5. Mild, chronic.	15. Chronic and appendicitis.
6. Chronic.	16. Chronic and adhesions.
7.	17. Constricted appendix.
8. Gangrenous.	18. Chronic and adhesions.
9. Fibrinous.	19. Constricted and adhesions.
10.	20. Chronic and adhesions.

TABLE VI.—Appendicitis. Blood.

Number.	Hemoglobin, per cent.	Red-blood cells.	White-blood cells.	Polynuclears.	Small lymphocytes.	Small mononuclears.	Large lymphocytes.	Large mononuclears.	Eosinophiles.	Basophiles.	Transitionals.
1	75	4,000,000	7,400	55.0	34.0	5.0	2.5	1.5	0.0	0.0	2.0
2	80	5,190,000	7,800	72.5	18.0	5.0	1.5	0.5	0.5	0.0	2.5
3	74	6,100,000	3,940	58.0	30.0	2.0	2.0	2.5	0.0	0.5	4.0
4	89	5,070,000	14,000	59.0	23.0	8.0	1.5	0.5	3.5	0.0	3.0
5	82	4,590,000	13,400	60.5	21.0	3.0	1.0	0.0	1.0	0.5	2.0
6	78	4,710,000	8,600	64.0	21.0	7.0	0.0	1.0	0.0	2.0	5.0
7	80	5,330,000	27,400	79.0	13.5	3.0	0.0	1.0	0.0	0.5	3.5
8	90	4,600,000	11,800	51.5	35.0	6.0	0.0	0.0	4.0	0.5	1.0
9	75	4,395,000	18,000	86.0	10.0	0.0	0.0	1.0	0.0	0.0	3.0
10	85	5,341,000	14,240	82.0	11.0	4.0	0.0	2.0	0.0	0.0	1.0
11	102	8,160,000	11,400	63.0	18.5	3.5	4.5	0.0	4.0	0.5	5.0
12	103	7,650,000	6,400	69.0	21.0	1.0	5.0	0.5	0.0	0.5	1.5
13	80	3,700,000	5,800	57.0	41.0	0.0	0.0	1.5	0.5	0.0	0.0
14	75	4,100,000	13,600	72.0	18.0	6.0	0.0	1.0	0.0	0.0	3.0
15	100	4,780,000	11,400	61.5	12.5	11.0	2.0	1.5	7.0	0.5	4.0
16	75	4,780,000	11,800	59.5	20.0	9.0	1.0	2.0	1.5	0.0	7.0
17	95	6,480,000	12,800	65.0	21.5	5.0	3.5	0.5	0.5	0.5	3.5
18	90	5,000,000	12,200	58.0	19.5	12.5	2.5	1.0	4.5	0.0	2.0
19	88	4,920,000	22,400	64.5	11.0	13.5	2.0	1.0	0.5	0.0	7.5
20	80	4,610,000	6,200	65.5	14.5	14.5	1.0	0.5	1.0	0.0	2.0

It is evident from Table V that 20 cases proved to be appendicitis. In nearly all the cases the stomach, duodenum, and pancreas were explored and were found to be normal. In doubtful cases the appendix was examined by the pathologist and found to be diseased.

In Table VI it will be seen that the average percentage of hemoglobin was 84, the average number of red-blood corpuscles 5,165,000. In 3 cases polycythemia was found, although the hemoglobin in 1 case (3) was much lower in comparison with the number of red-blood cells. The frequency of polycythemia in our cases of appendicitis would be as 3 to 20, or 15 per cent. In the remainder the number of red cells was normal or below normal. Leukocytosis was found in 13 cases, or in 65 per cent. and in 1 case leukopenia. The frequent occurrence of large mononuclears and the increase in tran-

sitionals should be noted. The large mononuclears were absent from the blood only in three cases of appendicitis.

Chief characteristic for appendicitis: Large mononuclears, transitionals, and leukocytosis.

One can see from all the tables that there is a relationship and difference in the blood of pyloric, non-pyloric and duodenal ulcers, and appendicitis. The blood in non-pyloric ulcer is related to the blood of duodenal ulcer so far as erythrocytes, lymphocytes, eosinophiles, and transitionals are concerned, but differs in regard to the number of leukocytes. The presence of leukocytosis in non-pyloric ulcer makes the blood in this condition related to appendicitis. The most striking difference is found between the blood of pyloric ulcer and non-pyloric and duodenal ulcers.

The difference in the morphology of blood led us to construct types of blood-pictures in the mentioned conditions: Pyloric, non-pyloric, and duodenal types. The blood-picture in appendicitis, although it has a special characteristic, large mononuclears, which were absent from the blood in the ulcers of stomach and duodenum, does not represent a special type, but it is a combination of types.

The accompanying diagram illustrates what is meant by types and by combined types: Three lines are drawn from points of the first portion of the duodenum, pylorus, and lesser curvature, cardiac portion. They all meet at a point of the appendix. The spaces between the lines represent the combinations. The following combinations are therefore possible in appendicitis: duodenal, pyloric, and non-pyloric; duodenal and pyloric; pyloric and non-pyloric; duodenal and non-pyloric.

We have selected of the many the following four cases to illustrate the value of blood-findings as interpreted by us in this paper for the differential diagnosis of the conditions discussed.

CASE I.—A. L., male, aged thirty-eight years, plumber. Patient is ailing with indigestion and severe attacks of abdominal pain for the last fifteen years. Pain starts in the pit of the stomach and radiates to right and left lumbar regions. He awakens at night on account of pain. Pain comes on from two to four hours after meals. His pain is relieved immediately after ingestion of food. He has never vomited, nor has he noticed blood in his stools. Has never been constipated. Appetite good. Physical examination: great tenderness to right at navel, none in the appendicular region.

Gastric analysis on fasting stomach; marked microscopic stagnation on one examination, absence of stagnation on a second occasion.

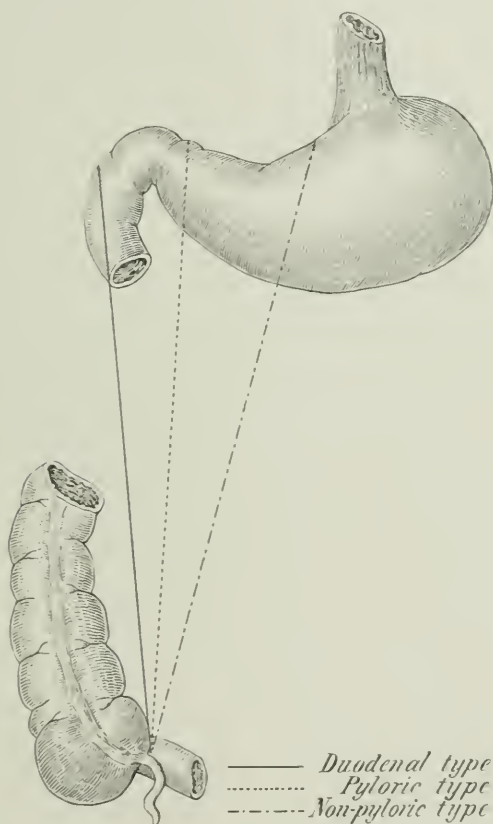
After test breakfast obtained 10 c.c. contents; hyperacidity. X-ray examination showed hypermotility of the intestines.

Patient gave a clear Moynihan's history; hunger, night pain, and late pain. Pylorospasm (intermittent stagnation), frequently found in duodenal ulcer, was present.

X-ray findings were also in favor of duodenal ulcer. Last, but not least, polycythemia was found (Case 2, Table VI).

Operation by Dr. Peck revealed a congested appendix and bands around. No ulcer in the duodenum nor in the stomach.

The blood-findings did not correspond to the duodenal type. They presented a combination of all the three types: polycythemia-duodenal type, relative eosinophilia (4 per cent.), pyloric, and leukocytosis, non-pyloric type.



CASE II.—K. H., aged twenty-five years, grocer, was seen first August 7, 1913. Patient complained for several years of attacks of spontaneous pain in the region of the left hypochondrium. Pain is at times sharp, at others gnawing. Lately pain comes on three to four hours after meals. He is always relieved from pain after ingestion of food. Never had pain at night. No vomiting. On several occasions he has noticed blood in his stools, and at one time he had an intestinal hemorrhage which lasted three days. Has been always nervous.

Physical Examination. Great tenderness in the region of left hypochondrium. Gastric analysis on fasting stomach; 20 c.c., bile-tinged. After test breakfast, 140 c.c. Volume of solids much larger than volume of fluids. Hyperchlorhydria. Urine negative. X-rays showed a residue of bismuth at the pylorus after six hours.

Blood (Case 13, Table VI) showed anemia and the presence of large mononuclears.

Patient was on Lenhardz diet two weeks and later under ulcer therapy. He improved considerably for a short time, but in October he began to vomit repeatedly and in November he again had a severe intestinal hemorrhage. His feces, examined several times, gave positive reactions with guaiac.

About one month later, after recovering from his hemorrhages, he was referred to Roosevelt Hospital for operation, with the diagnosis of gastric ulcer. The operation, which was performed by Dr. Peck, did not reveal any ulcer in the stomach nor in the duodenum.

The blood of this patient was examined a number of times. On one occasion only it showed 5,100,000 after he had vomited for about a week several times a day. The smears repeatedly showed the same picture; large mononuclears, absence of small mononuclears, and scanty eosinophilia.

A correct diagnosis could have been made in this case if the history and symptoms and signs had not been overestimated and blood-findings underestimated. The blood did not correspond to any of the chief types, but presented a mixed type; from pyloric anemia, absence of small mononuclears, and scanty eosinophiles, as in the cases of the non-pyloric and duodenal groups. Large mononuclears, one of the characteristics of appendicitis, were present in the blood.

CASE III.—W. D., male, aged forty-three years, tailor, was seen first August 20, 1913. Five years ago patient began to have sharp, cutting pain in the right lumbar region, which radiated to the left of the abdomen, chest, and back. They usually lasted from one-half to two hours. The pain never came on at night or in late hours after ingestion of food. The pain was always relieved after meals. For the last two years the pain has become continuous. He vomited only twice since his present illness started. Never had hematemesis or melena. Appetite fair. Bowels regular.

Physical Examination. Corneal anesthesia. Loss of pharyngeal reflexes. Slight tenderness around right side. No muscular rigidity. Gastric analysis: No stagnation of food. Mild hyperacidity.

Feces: No occult blood.

X-ray examination negative.

Operation (Dr. A. A. Berg) revealed a double ulcer (duodenal and gastric at lesser curvature) near cardia. It was difficult to induce the surgeon to operate upon the patient for duodenal

ulcer. Except hunger pain there was nothing to account for the diagnosis. However the blood-picture showed the full duodenal type with leukocytosis, which was present in all the cases of the non-pyloric group.

CASE IV.—S. M., aged forty-seven years; tinsmith; was first seen December 14, 1913. Until six weeks ago he was perfectly well. About that time he was suddenly seized with abdominal pain and constipation. The cramp-like pains came on every five minutes. Pain was not relieved after taking food. He has never vomited. Had bleeding piles. Has lost in flesh.

Physical Examination. Tenderness in the region of the colon descendens. No tenderness in the epigastric region, nor elsewhere in the abdomen. Digital, rectal, and proctoscopic examinations negative. The blood (Case 4, gastric ulcer, Table II), pointed to the non-pyloric type. The introduction of the stomach-tube was refused by the patient first and allowed later.

Gastric analysis showed stagnation of food and hyperacidity.

X-ray examination showed a bismuth residue after nine hours.

The history of the patient led one rather to suspect malignancy of the sigmoid; a sudden onset of attacks of abdominal pain, and constipation with localized tenderness in lower abdomen to the left in a man in the carcinomatous age.

Gastric analysis and x-ray findings pointed strongly to pyloric obstruction of non-malignant character.

The operation (performed by Dr. Peek) revealed an indurated ulcer at the lesser curvature two inches from the pylorus, which was found to be patent. It is evident that positiveness was obtained by the aid of blood-findings.

We have purposely refrained from the discussion of the diagnostic signs and symptoms hitherto known in these conditions. In our hospital and private practice we have of course followed them, but we never obtained such definite indications as we have since we have made careful studies of the blood such as are indicated above. Of course the history, the physical examination of the abdomen, the analysis of the gastric contents and of the feces, and finally the x-ray findings give valuable data; none of these, however, seem to stand in definite relation to the site and character of the lesion in the great majority of cases. The blood-findings, on the other hand, seem to possess such a relation, much as the changes in mentality, in muscular strength, and in reflexes, bear a definite and localizing significance in the diseases of the nervous system.

NOTE.—In Cases 17 and 18 (Tables III and IV), owing to our interpretations of blood-findings, the diagnosis of duodenal ulcer and appendicitis was correctly made and with these diagnoses the patients were referred to Dr. Peek for operation.

MYOPATHY: WITH CLINICAL RECORDS OF EIGHT CASES COMPRISING VARIOUS TYPES.

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THE myopathies have been widely discussed of late years, both abroad and in America. Last year the study of this subject was stimulated by a paper by William G. Spiller,¹ which was laid before the Neuropathological Section of the International Congress. In it he discussed the relation of the myopathies and the classification of the various types.

The present paper contains clinical records of eight cases. There are no postmortem findings, as all the patients are alive. In one case (Case VI) there are biopsy findings which reinforce the diagnosis.

The results of a study of these cases only emphasize the meager benefits that may be claimed for any method of treatment that has been tried. The diagnosis in Case VIII is tentative. The condition being a rare one and the symptoms having recurred after a remission of five years, it must needs be guarded until further developments occur.

CASES I and II.—Atrophy combined with pseudomuscular hypertrophy. Referred to me by Dr. Charles L. King, of Pasadena.

Two brothers, G. C., aged eleven years, and J. C., aged nine years.

Family History.—Both parents are alive and healthy. There is no history of similar disease on either side of the family. There are four other children (three girls and one boy), all of whom are thus far normal; one boy is aged thirteen years, one girl fourteen years, one girl six years, and one girl three and one-half years.

CASE I.—Corresponding to the Werdnig-Hoffmann type.

Previous History.—G. C., aged at present eleven years (seen first in 1911; last time in 1914). All during his intra-uterine life his mother's health was bad; she suffered with asthma and was given large doses of strychnin daily. He was born at term, but never could crawl. The first attempt at locomotion was standing by a chair and pushing it ahead of him. He did not walk alone until about two and one-third years of age. He had adenoids, which were removed. He was circumcised. As a baby he could never sit alone.

Present Condition (1911). He cannot walk or run like other boys, and is easily pushed over. His parents say that his condition

¹ Brain, vol. xxxvi, Part 1.

is progressing badly. While he has been under my care he developed pneumonia, from which he recovered.



FIG. 1.—Case I (a).

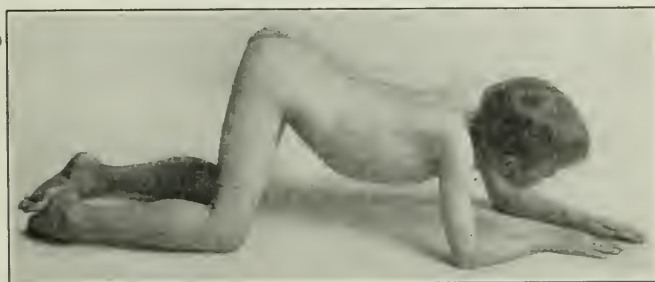


FIG. 2.—Case I (b).



FIG. 3.—Case I (c).

Physical Examination. Gait is waddling. When he lies prone and attempts to arise he does so by means of a characteristic sequence of mechanical acts (see Case I, Figs. 1 to 5).

Lordosis is present to a noticeable degree. His superior maxillary and palatine arch are very high and his teeth present irregularly.

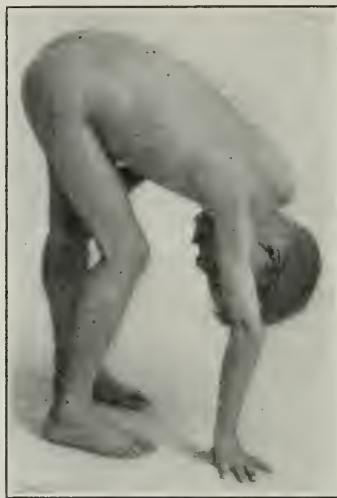


FIG. 4.—Case I (*d*).



FIG. 5.—Case I (*e*).

therefore his speech is affected and he lisps certain sounds. Also, his speech is processional. His scapulae flare. When he is raised from the ground by means of hands placed in his axillae the shoulders

are pushed as high as his ears before his feet begin to leave the ground.

He exhibits inability to flex the feet, difficulty in flexing either thigh, difficulty in raising erect from a stooping posture.

The calf muscles appear to be very much hypertrophied. They are large and hard, but lack strength (see photographs). Reflexes: knee-jerks absent.

During the three years he has been under observation his condition has not improved, but rather decidedly progressed. During that time the calf muscles have increased in circumference 4 cm., whereas the thighs have decreased 2 cm. The progress of his disease has left him almost helpless (1914).



Case I.

Case II.

FIG. 6.—Note double foot-drop.

CASE II.—*Pseudomuscular hypertrophy of the Duchenne type of dystrophy.*

J. C., aged eight years (seen first in 1911; last time in 1914).

Previous History. He had three or four "spasms" while teething, but none since. While he was under my care he, with his similarly

afflicted brother, developed pneumonitis. It was considered quite a triumph to have them both recover. Almost their sole medication during this infection was quinin in suitable doses.

Present Condition. He cannot run quite like other children. It is especially difficult for him to ascend steps, except with assistance. His ability to play and get about is much better than his brother's, but his gait is waddling.



Case II.

Case I.

FIG. 7.

Physical Examination. His general muscular development looks excellent (see photograph), but he stumbles easily and cannot flex his thighs effectively. He can flex his feet. When he arises from the prone position the act is accomplished much more easily by him than by his brother. Since he was first seen (1911) his condition has not progressed nearly so rapidly or to such a marked extent as his brother's.

CASE III.—*Infantile dystrophy.*

D. P., aged twenty-eight months, seen in my service at the Children's Hospital.

Family History. Father died of tuberculosis. Mother has had malaria, but is now in good health. No other members of the family are affected like the patient.

Previous History. She was born at full term and without instruments. Her health has been good. When she began to crawl she seemed strong and active, but it was noticed that she was stronger in the right leg than in the left. She did not walk until she was fifteen months old, and for a time she walked very well.



FIG. 8.—Case III.

Present History. For the last two months she has become weaker steadily. This shows itself especially in her locomotion.

Physical Examination. The child is apparently well nourished and her musculature looks above rather than below the normal. But, whereas the anterior portions of her thighs, for example, look large and strong, a firm grasp reveals in reality a soft, flabby struc-

ture. The calf muscles are similarly deceptive. The dorsal muscles are weak and the child stands in the position of lordosis. Her gait is a succession of weak efforts and she will fall unless assisted. The muscles of the arm and shoulder are quite strong. The joints of the ankles, knees, and wrists are extremely pliable. Reflexes: The knee-jerks are present but sluggish.



FIG. 9.—Case IV.

CASE IV.—*Myopathy coming on in adult life, remaining stationary after a period of progression.*

Mrs. H. W., aged thirty-eight years. Colored. Seen in my service at the Dispensary of the University of California, Los Angeles Medical Department.

Family History. Father is alive and healthy. Mother died of nephritis. They had seventeen children; of these nine lived. Eight died in early childhood (patient did not know if any of them exhibited symptoms of muscular dystrophy).

Previous History. Typhoid pneumonia at about eight years of age, otherwise she has been healthy. She says that she could run and jump much better than most girls. She has been married twice, but was never pregnant.²

² Suggesting luetic infection.

Present Condition. About seven years ago she noticed a beginning inability to run fast. Later she found that she could not go up stairs as easily as before. Still later her back became weaker; she could not lean forward without taking hold of her own knees; she could not arise from a prone position or stoop to the floor without "climbing up her own legs."

Physical Examination. Pupils equal and react normally. Gait is waddling. Station is good. Reflexes: Knee-jerks sluggish; ankle-jerks absent. No Babinski. Sensation intact.

The leg muscles looked very strong, but she exhibited difficulty in flexing the thighs against pressure. There was marked lordosis (see photograph).

Since seeing her first the condition has not progressed and she thinks it has remained stationary for over a year.

CASE V.—*Progressive atrophy of the shoulder girdle, dorsal, thoracic, and thigh muscles, with true hypertrophy of the calf muscles.*

X, aged twenty-four years. Referred by Dr. A. S. Lobingier and seen in consultation with him and Dr. Harvey Cushing.

Family History. No evidence of a similar disease in his family.

Previous History. Has always been well except for the present trouble.

Present Condition. This began in early adult life and has steadily progressed until he is now unable to walk, except in the most grotesque and seemingly impossible manner, because of the extensive involvement of the lower dorsal and thigh muscles. There has been no pain or discomfort in the muscles themselves.

When he walks he cannot move forward in the direction in which he seems to be facing, but is forced to walk to his destination sideways and with a succession of spasmodic movements of his legs which would be absolutely impossible for him, except that necessity has forced him to learn them because of the gradual loss of one set of muscles after another and their adoption has been a forced selection. His condition is truly pitiable and especially so as he has lately married. His only possible mode of getting about is by wheel chair. We strongly advised him against having children.

CASE VI.—*Progressive atrophy, beginning in the trapezius.*

W. M., aged twenty years; machinist. Referred to me by Dr. MacKerras, of Sierre Madre, California.

Family History. Both parents are alive and in good health.

Previous History. He had measles when a young child, otherwise his health has been exceptionally good. Five years ago he began to work in a machine shop and did not notice any abnormality up to two years ago. In his work he has carried heavy weights.

Present Condition. About two years ago he began to experience momentary spasm in the muscles of the right side of his neck, which at times were severe enough to draw his head to that side.

They would come on at irregular intervals, at times daily for many days. At present this will occur only occasionally and with long intervals between spasms. He began to notice that the right shoulder was lower than the left at about the same time that the spasms began. At present the spasms are very mild.

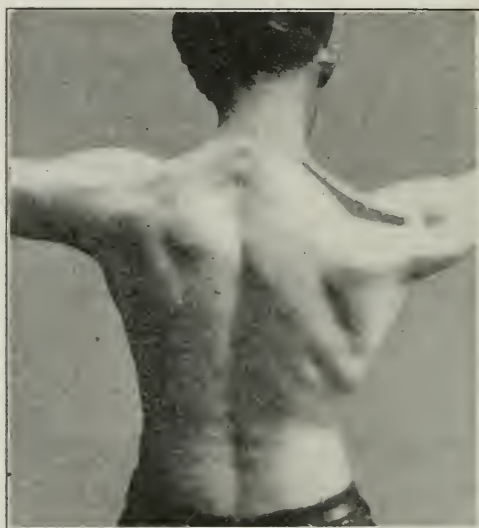


FIG. 10.—Case VI.

There has been no pain or tenderness in the affected muscles, but he has been conscious of a tired ache in them that has been fairly constant for some time. The wasting has been progressive and has not affected the strength of any other muscles than the trapezius and the clavicular branch of the sternocleidomastoid (the affected muscles) (see photograph, Case VI). The affected muscles feel putty-like under the fingers.

The treatment in this case was the application of the faradic current daily through a period of six weeks. The effect of this treatment was beneficial as far as the subjective symptoms of tiredness and aching were concerned. There was some real filling out of the scapular and adjoining muscles, upon which extra strain was placed because of the impotence of the trapezius.

A biopsy was performed; the portion of the trapezius examined showed the typical proliferation of nuclei in the muscle fibers, with disease of the muscle fibers and surrounding tissue.

CASE VII.—Progressive neurotic muscular atrophy.

J. S., aged fifty-six years. Referred to me by Dr. C. H. Lowell.

Family History. Both parents and all their eight children are gouty. None of them show a condition similar to the patient.

Previous History. Up to four months ago he was in good health. In July, 1913, he was in a serious railroad wreck, but did not exhibit any nervous symptoms for five months.

Present Condition. In November, 1913, his leg muscles began to become stiff, tender, and weak. He began with difficulty in flexing his thighs, as in ascending steps. Later he began to stumble, due to difficulty in flexing his feet. He stubs his toes frequently and almost falls. Once he caught his right toe back of his left ankle and nearly fell.



FIG. 11.—Case VII.

Lately his locomotion has been greatly interfered with because of intense fatiguability in the legs, almost identical with that of intermittent claudication. The right arm has begun to be affected, and he is now unable to raise his hand above his head or place it at the back of his neck. He cannot use his fingers as in the act of buttoning. When he walks he drags his right leg more than his left, though his left is very weak also. His weight has decreased rapidly.

Physical Examination. Pupils equal and react normally to light, and in accommodation. The tongue is protruded well but slightly to the right; it shows no tremors.

There is no tremor of the face. Lightning-like fibrillary tremors are noted in the arms, thorax, and legs. His grip is good in both hands, but relaxes soon.

Station is unsteady with eyes open or closed.

The thighs are wasted and the flexor muscles most affected.

The feet cannot be forced beyond the walking angle.



FIG. 12.—Case VII.

The calf muscles are tense and contracted, and give the sensation of being hard and indurated to the palpating hand.

Reflexes exaggerated. Tapping over the muscles causes them to jerk.

When the patient lies prone and the left leg raised, he experiences sudden cramp-like pain in the deep flexors of the upper thigh.

This case seems to correspond to the neurotic type of progressive muscular atrophy as described by J. Hoffman in *Die Deutsche Klinik*.

CASE VIII.—*Myasthenia, especially of extra-ocular muscles.*

R. P. S., aged thirty-two years; married. Referred to me by Dr. Lewis Thorpe.

Family History. His father died when the patient was six months old, after an operation for cancer. His mother is alive and healthy. No other members of the family are afflicted as he is.

Previous History. He has always been healthy and athletic, except that five years ago he had a right hyperphoria lasting five months. At that time he was under the care of Dr. Lewis Thorpe, an oculist. After a trip to the mountains this condition seemed to disappear. There were no accompanying symptoms.

In May, 1913, he was infected with gonorrhea and was discharged cured in six months (see below).

In August, 1913, he began to notice a disturbance of vision when he looked to the left. This was a temporary diplopia. In December following he noticed that in addition to this the left eyelid would droop and the left eye-ball showed a tendency to look downward and outward; this came on within forty-eight hours. Both eyes were more or less similarly affected, but the left one more than the right. He then went on a two months' trip, as he had become very weak and nervous. For a time he experienced various sensory disturbances, for example, numbness and stiffness in the face, head, arms, and legs. There was no headache, nausea, or vomiting, nor has there been at any time since.

In February, 1914, the disturbance of vision became worse, due to progressive weakness in the extra-ocular muscles, especially the right external rectus, both internal recti, both superior recti, and left levatory palpebræ superioris. The right levator palpebræ superioris was affected, but to a lesser degree. His symptoms are decidedly aggravated after any excitement.

In addition to the myasthenic condition of the extra-ocular muscles he complains of fatiguability that is more or less general. This does not show itself in any speech disturbance or marked weakness in any one set of muscles, and it is not constant, although he never feels the normal capacity.

Physical Examination. Pupils are equal and react to light and in accommodation; convergence is impossible for him. When asked to fix a line he will see one end of it bent downward. Continuing to fix it will result in the ability to do so. He can overcome the diplopia by an effort. The excursions of the eyes vary at different times. The excursion of the eyes in conjugate movements is not the same (for each eye) as when they are tested separately. For example, when both eyes are moved together the unequal pull on the muscles is not apparent; when they look to the left the external rectus does not pull the left eye outward to the same extent as when the left eye is abducted alone, and as it would do if the nerve to the left internal muscles was paralyzed. Similar differences are noted in other movements. This point was considered to be of sufficient diagnostic importance to help rule out nuclear and neural involvement and to enable one to locate the disease in the muscles. The picture is a different one from ophthalmoplegia externa due to syphilis or neoplasm.

Ptosis is noted on both sides but more pronounced on the left. The extent of ptosis on both sides varies from time to time and at times is scarcely noticeable.

Although he complained of fugacious feelings of stiffness and numbness in the face it was not possible to discover any disturbance of function in the distribution of the facial or trigeminus on either side. Station and gait are good. Reflexes: biceps, knee, and Achilles-jerks are somewhat exaggerated. There is no Babinski.

Heart and lungs are normal. Blood-pressure is 125 systolic.

The eye examination (by Dr. Lewis Thorpe) showed normal fundi.

An instructive feature of the examination of the color fields is that the first two examinations showed some interlacing and did not conform to each other. The third one was normal. The reason for this was that he was overanxious to obey instructions, and, until this was discovered and corrected, he gave faulty answers.

Repeated examinations seem to be essential.

Laboratory examinations (by Drs. Brem and Zeiler): Wassermann (blood and spinal fluid) negative. Von Pirquet skin test for tubercle bacilli negative. Noguchi luetin test negative. Complement-fixation test for gonorrhea positive.

In this connection it is to be remembered that his first myasthenic attack was nearly five years previous to the gonorrheal infection. Whether the presence of a toxic focus that is surely active is sufficient to have a determining effect upon the recurrence of the myasthenia remains to be seen. Neoplasms, nuclear disease, and the various forms of encephalitis and meningo-encephalitis seem to have been eliminated. The same is true of tuberculosis and syphilis of the central nervous system. Therefore a tentative diagnosis was made of myasthenia of the extra-ocular muscles with a less-marked general involvement. Myasthenia gravis pseudo-paralytica may be the final diagnosis. The dominant symptom is the ready fatiguability of the extra-ocular musculature. The condition is progressing unfavorably.

The treatment in this case is the exhibition of thymus gland, strychnin, and electricity.

SUMMARY. Case IV is the only instance known to the writer of myopathy in a colored person. In this case there has been an arrest of the condition for over a year.

The electrical reactions in every case were a very much delayed response to the faradic interrupted current in the affected muscles.

Two of these cases were brothers, but in no other case was the familial element present. In none of them was there a history of heredity. The exhibition of electricity was distinctly beneficial in at least one case (Case VI).

Little or nothing that was elicited in these cases could be considered in the light of an etiological factor except muscle strain in Case VI and general exposure in Case VII.

THE USE OF PITUITARY EXTRACT IN THE CONTROL OF SOME OF THE ASSOCIATED SYMPTOMS OF PNEUMONIA WHICH FAVOR HYPOTENSION.

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THE emphasis in the therapeutic use of pituitary extract in pneumonia has, thus far, been chiefly laid on its marked stimulating effect on the circulation and in the enthusiasm engendered by this discovery, other effects favorable in certain emergencies of pneumonia have been overlooked or remained unmentioned.

With our present knowledge as to the significance of the blood-pressure in pneumonia every factor bearing on this phase of the question deserves close attention. While it is true that all depression of blood-pressure in pneumonia can be traced to the effect of the pneumonic toxin directly or indirectly on the circulation, yet much can be gained from an analysis of the way in which various factors affecting the course of the disease in this way act. As examples of factors acting unfavorably in a general way, lack of fresh air, improper or insufficient nourishment, excessive cough, pain, loss of sleep, etc., may be mentioned. Without minimizing the importance of such factors, should, however, factors present themselves which in addition to their general capacity for harm manifest a specific action on the circulation, our interest should be doubly aroused. It is to two such conditions at times associated with pneumonia, tympanitic distention and diarrhea, that we desire to call attention.

Tympanitic distention presents a comparatively simple problem. The circulation is hampered in a twofold way. The diaphragm is forced upward so that not only does the capacity of the chest at rest suffer, but its active capacity is curtailed through inability of the diaphragm to descend freely on inspiration. This results in impaired oxygenation of the blood, a lack which is magnified by the added demands of the increased effort in breathing. The heart, in turn, nourished by this oxygen-poor blood, is less able to perform its task and is further hindered by the crowding and change of position to which it is subjected.

The cause of the distention is a more or less complete paresis of the intestine, toxic in origin, and directly dependent on the pneumonic poison. How remedy this state of affairs? The course which suggests itself—reduce the dose of poison by elimination—cannot practically be followed as a first step. The reason for this is obvious, the organs to which we must turn, the lungs, the skin, the bowels, and the kidneys, are already seriously handicapped or their use contra-indicated. In the lungs hampered, as described

above, the futility of hasty respiratory stimulation is apparent. The skin offers no hope of assistance, as relaxed and sweating states must be avoided. The bowel, the seat of the trouble, we presume would not present this condition had efforts already directed to its support have availed. The kidneys, dependent as they are on some degree of circulatory efficiency, must be discounted as our circulation is throttled by the very symptom we are trying to relieve. Thus it seems that a blank wall is met, and it is for this reason that we justly view with alarm the syndrome of weakened heart sounds, rapid, compressible pulse, drooping pressure, dyspnea, restlessness, scanty urine, constipation, and gas-distended bowel.

The relief of the tympanic distention, all will agree, is here the thing above all to be sought. Rather relieve the distressing symptom by measures directed specially toward it than to practice a still further stimulation of a collapsing circulation. When the condition is marked it is too late to invoke diet; it is too late to lessen toxicity. These questions should have been to such an extent under the physician's care prior to the onset of this symptom, that little were left to be done in this respect. The hope of successful emergence from the dilemma depends upon the extent to which direct measures to the relief of this tympanites have been exhausted. It is not our purpose to speak of the use of carminatives by mouth and by rectum, supplemented by the rectal tube, local applications to the abdomen, and the hypodermic use of strychnin, eserine, etc., but rather of a single, newer therapeutic agent which in our experience will accomplish the desired result when our other most trusted measures have failed. We refer to the extract of the posterior lobe of the pituitary body. This as obtainable under the trade names of pituitrin, hypophysin, etc., ready for hypodermic use, offers no technical difficulties in its administration.

Its stimulating effect on the intestinal muscle,¹ a property too often overlooked, is now called upon. There is nothing bizarre in this action, the unstriated muscle of the intestine is simply sharing this effect in common with such involuntary muscle as that of the uterus and arterioles. The dose of 1 c.c. can be given subcutaneously and repeated at one, two, three, or more hour intervals as the need arises. In the graver cases more is to be feared from a persistence of distressing symptoms than from untoward effects from an overdose. The preparation has been shown to be non-toxic, and should conditions be such that it can do no good it should certainly do no harm. When administered in sufficient dose the effect is indeed gratifying. Where no passage of gas is obtained before its use, such passage often soon takes place, even at times to the extent of loud and repeated flatus. The general circulation

¹ Bell and Hicks, *British Med. Jour.*, March 27, 1909; T. W. Harvey, *Med. Rec.*, March 21, 1914.

benefits not only from this release, but is itself independently stimulated and toned up. Indeed, one must not lose sight of the fact that this circulatory awakening may have carried such previously administered remedies as eserine and strychnin to their goal and so added their beneficial though tardy effect. The mental as well as the physical condition of the patient quickly responds, and the picture from one of despair and exhaustion is turned to one of hope and comfort.

Needless to say, elimination by the bowels, kidneys, and lungs is reestablished in a favorable case and the underlying cause of the trouble is relieved, even though it be secondarily. It is fair to assume that no procedure, had it not attacked the intestinal relaxation with equal vigor, would have prevailed. The greater effect on the intestinal musculature, in the presence of tympanites, of this substance than that obtainable from any other agent is paralleled by its similar greater action on the arterioles and uterus. In all these instances its effect seems to be the most beneficial when the need is the greatest. The diuretic action of pituitary extract should be mentioned in passing. Its bearing on the problem of elimination is of course apparent.

Diarrhea in pneumonia presents another condition in which in addition to its general exhausting effect on the system it singles out the circulation and lowers blood-pressure by the extraction of fluid from the circulating blood. The problem differs from that in the case of tympanites in that up to a certain point the diarrhea may be considered as advantageous in the exercise of the eliminative function of the bowel.

It must be decided first, therefore, before thought is given to therapeutics, whether the diarrhea is increasing or decreasing the patient's chance of recovery. Our chief guide here, as in the other emergencies of pneumonia, must be a study of the state of the circulation. When it can be shown that the vigor of the circulation is lessening it would seem by far safer to assume that any advantage accruing from the continuance of diarrhea will be more than overbalanced by the harm it may work. In such case it should be controlled, but by this is not meant a near stoppage of elimination by this route. Provision should be made for adequate but not excessive bowel movement.

For years clinicians have realized the value of the bowel as an aid to elimination in pneumonia, but while advising of its use have cautioned against its abuse. The present discussion does not presume to add anything to this advice, but simply hopes to make its application more simple by correlating the blood-pressure phenomena and elimination by bowel in such a way that an instrument of precision may be brought to the aid of our only too often inadequate, clinical sense.

The diarrhea may be a true eliminative one and thus compensa-

tory to the action of the kidneys. It may be irritative as the result of bacterial and other changes consequent on the perverted alimentary function at such a time or due to improper feeding or medication. It may also be a true relaxing diarrhea associated with a general systemic depression.

In the first instance it may be distinctly helpful; in the last decidedly harmful, and in the intermediate instance either helpful or harmful, depending on whether the gain to the system in ridding itself of noxious material is not counterbalanced by an excessive fluid loss.

While it can be stated that any marked diarrhea will lower the blood-pressure it cannot likewise be stated that such fall will invariably work harm to the patient. This is specially true during the early hours of the disease when congestive phenomena are present and a general plethoric condition exists. At such a time free catharsis may take the place of the less safe use of such depressants as *veratrum viride* or *aconite*.

As illustrative of this fact the case comes to mind of a stout, middle-aged man recently seen who early in the course of pneumonia showed flushed face, overfilled vessels, rapid, bounding, and occasionally irregular pulse, moderate dyspnea with a systolic pressure of 180 mm., and a diastolic pressure of 110 mm. A course of calomel, followed by free saline catharsis, resulted in a fall in systolic pressure of 20 mm. and in diastolic pressure of 25. mm., together with other evidences of improved circulatory conditions. This fall must not be considered a fall from but a fall to normal for this individual. Later also if the blood has accumulated in the venous side of the circulation and the right heart is laboring and blood-letting is indicated free catharsis in the absence of this salutary measure would seem to be indicated. In this event what the circulation calls for is depletion.

When the primary excitation is passed and the toxins of the disease are about to manifest their depressant effect the presence of diarrhea must be watched with distrust. The circulation having subsided from its first reaction to the invasion, the normal (for the particular individual) systolic, diastolic, and pulse pressures should be ascertained and then watched.² The pulse blood-pressure ratio should be followed and changes in the auscultatory sequences observed.³ Should an undue looseness of the bowels then exist in the presence of sphygmomanometric evidence, than which there is none earlier of lessening circulatory efficiency, this condition should be brought under control.

Again it is not our purpose to consider the usual means to this end. In connection, however, with what has been said of the

² Nicholson, AMER. JOUR. MED. SCI., April, 1914.

³ A. A. Howell, Jour. Amer. Med. Assoc., April 18, 1914.

action of pituitary extract on the intestine it is an interesting question to decide whether or not its administration is contra-indicated by the presence of diarrhea. I feel that it is not. While it has undoubtedly a stimulating action on the intestine, this will not unduly manifest itself in the face of an already existing motor excitation. Nor does its introduction into the system entail a further pouring of fluid into the intestine; quite the reverse should be the case, through the improvement of vascular and general tone. The exhibition then of pituitary extract, if it is indicated for circulatory reasons, is not contra-indicated by the presence of diarrhea. When a satisfactory bowel condition has been reëstablished special care should be exercised in the nourishment of the patient and provision made for as free elimination as possible through the kidneys.

It is not essential to the value of the action of pituitary extract whether it be considered as a true internal secretion or not. Suffice it to say that in the posterior lobe of the pituitary body an adrenalin-like principle is contained which, due to its special organic structure, produces and maintains rises in blood-pressure better than does adrenalin, and therefore is more reliable in conditions of circulatory collapse than is adrenalin. Also in addition to this action its selective action on involuntary muscle as a whole should not be overlooked, and more especially in the present connection its stimulating action on the intestinal musculature.

THE TRAUMATIC NEUROSIS.

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PHYSIOLOGICAL FUNDAMENTALS. Traumatic neurosis is a complete misnomer; the condition is psychogenetic, therefore it is not neural; and the trauma is not physical. An injury in itself cannot cause a "neurosis," meaning a psychosis. This condition occurs only when the patient broods over the injury and imagines that he is a very sick person. To represent to oneself feelingly a disease is to make oneself feel very sick, even although the disease one conceives may not itself be manifested with verisimilitude. The patient then, having the idea that he is sick, acts so and feels so; so that after a while he actually is sick.

This is on account of the fact that the idea of pain is capable of arousing the concomitants of pain, namely, depression of vegetative functions. This occurs because of the emotional reactions

inseparable from the concepts which experience has associated with them. The situation is merely that of the dog in which Pawlow, during his experiments, suppressed the flow of gastric juice by merely showing a whip. It is a "conditioning" of a reflex, and is feasible with any dog.

This fact makes manifest how erroneous is the common opinion that the "conditioning" of affective reactions in a morbid fashion requires previous morbidity for its accomplishment. This is usually stated in the formula that traumatic neurosis occurs only in the predisposed. The real factor in its induction is the momentum of the conditioning stimulus. A homely illustration is that used by the penetrating dramatist Augustus Thomas, in *The Harrest Moon*, where he makes a hard-headed lawyer, against his will, the victim of the suggestion that he is dangerously ill.

Of course it should be obvious that the patient, although a victim of imagination, may become really ill physically; just as it is obvious that Pawlow's dog, a mere victim of imagination, is ill therewith to the extent of an incapacity to secrete gastric juice, which means very ill indeed. Indeed, psychogenetic physical illness of this kind may reach such a degree as to cause death, as has been experimentally shown by Crile and others.

Furthermore, if the reactions have gone too far the removal of the cause will not save the life of the animal. Short of death, secondary organic changes may occur, so that recovery will be incomplete.

But even when the stimuli are insufficient to produce organic changes the cure of the subject demands more than a mere material removal of them, for the stimuli live in memory, where they have become associated with many elements of the environment; so that the cause is not really removed until a complete reconditioning is effected of all the associational reactions which have gathered around the initial dread-bringing circumstance.

For instance a tachycardia produced by fear, if long continued, should not be less injurious to the heart and bloodvessels than is excessive athletics; an outpouring of an excess of substances from the adrenals should just as likely produce vessel sclerosis or exhaust the gland when it is the result of chronic anxiety as when it is due to a physiological stimulus of more direct kind; a dyspepsia or chronic constipation is just as likely to lead to malnutrition and toxemia when it is the result of mental depression as when it is due to sluggish habits or some disease.

The mechanism by which the modification of reaction occurs is usually that of suggestion. The dog which secretes gastric juice when it hears a bell does so because of the suggestion that meat will be presented him forthwith. It does not know why a bell brings meat; it mistakes it for a reaction of cause and effect, like that of a wetting when it enters the water. The process is not one of

genuine reasoning. The person who is hypochondriacal after an accident has as little reason in calling accident cause and neurosis effect as has the dog in believing bell cause and meat effect. It is belief without proper ratiocination, received blindly, credulously, from someone else without criticism; that is, by suggestion. This is, unfortunately, the commonest method by which opinions are acquired by human beings. Indeed the vast majority acquire their beliefs in no other way; and only a few scientists and still fewer superior minds have eliminated this manner of appraising the facts they encounter. It is small wonder then that the conditioning of reactions becomes morbid so easily, for we find morbidity all around. It is often dramatically impressive and frequently comes home to us by association with the deepest affections. Hysteria, then, which is merely the "effects of suggestions when these cause disease," is necessarily very widespread, and the circumstances that give rise to it and the forms that it takes are proportional to their impressiveness, which means suggestive power, and in accordance with fashion and the *zeitgeist* of the country and time.

The mechanism is always the same, and the victim is not aware of the systems of ideas and associated affects which constitute his psychosis.

THE INDUCTION OF SUGGESTION PSYCHOSES. THE EMOTIONAL CONSEQUENCES. CASES AND DISCUSSIONS. In the gross these are most clearly manifest in what our attitude of detachment easily enables us to label the superstitions of alien peoples. Thus the sufferings induced by the "gnawing fox" of the Japanese are made possible only by a deeply rooted belief in its existence. For example, a woman after labor declared she felt the "fox coming," this was her interpretation of the after-pains she felt. The great parade by the neighbors in attempting to prevent the fox's attack only reinforced the patient's apprehension, and soon a horrible convulsion signaled her seizure by the fox. Terror and convulsions held her until the exorciser was called. He declared that the fox would leave her at four o'clock the next day provided certain offerings were placed on a certain tomb for it to eat. This simple suggestion caused her to dismiss her terror suddenly at the hour designated. The crudeness of the mechanism in the case of this ignorant peasant need not make us smile, for our Western case is very little better, as the following illustration shows:

It is the familiar case of an incapacitated railroad employee to whom we were called to determine whether or not there was organic disease of the nervous system. The fact that there was not is shown elsewhere in the full report of the case. The psychogenesis of the man's condition was evident in his fixed idea, due to the common belief of railroad employees that serious nervous disease may slowly ensue upon an accident. This common belief was strengthened by the injudicious sympathy and inquiries of his friends and the

doubtful prognosis of some medical men he had consulted. He "answered a thousand questions a day," he "did not know what to think about his health," and worried about his condition and circumstances; he was "too much preoccupied with his health even to miss his wife;" he had lost weight and appetite, had a sore throat, and wept much; and finally his attitude was strengthened by lawyers who sought redress for him. He was cured within a month as a result of one interview, during which he was instructed in the role of ideas over bodily activity and the effects of worry and anxiety upon nutrition. In the certificate it was stated "there is and has been no disease of the spinal cord or peripheral nerves at play in the induction of any of the symptoms which I find. The erroneous belief that there has been such an injury powerfully contributes to the anxiety which maintains his present state."

The role of the idea of shock in perturbing this man's emotional life is strictly comparable with that of the gnawing fox of the Japanese folklore. In both cases too there was the period of reflection and incubation of the morbid notion, a familiar feature of such cases which has been insisted upon by Souques. It is rare that the symptoms ensue until after a time of meditation, during which the complex is systemitized.

The cure was not so simple as that of the Japanese exorcist. But it was a definite one, for the railroad breakman was taught to understand the mechanism of his affection and thus to overcome any future harm from the credulity in which he had grown up.¹ The Japanese woman, on the other hand, remained liable to another attack, as her belief in the fox was only reinforced by the manner of its removal.

A contrasting case where therapeutics failed will further push the lesson home. A government employee was injured by a falling case and remained barely able to walk even after his bruises of head and shoulder had healed. Called in consultation we explained the mechanism of his present incapacity and directed how to remove it. His family physician's acquiescence to our directions was only formal, as his bent was not psychological enough to grasp the principles at work. The fearful solicitude of the man's wife too constantly reinforced his timidity, so that in spite of a considerable temporary improvement he did not progress to full recovery, but remained lacrymose, depressed, and relatively incapable on account of the persistence of his false belief about his health and powers.

LOSS OF "NERVE" AFTER AN ACCIDENT. Again, a railroad freight conductor was sent to me for care from North Carolina by the Southern Railway Company. He had fallen off a truck and had been much shaken and bruised. Unlike most persons in such case he did not complain of pain or paralysis, but merely stated,

¹ Five years later the man continues at work, well.

what was truth, that he "could not sleep, and remained in a state of nervous agitation which would even cause him to cry at times and made life unbearable, from incapacity, weakness, and mental depression, so that he felt utterly unable to return to work, feeling that he could not perform it." In his happy domesticity there were no extrinsic psychological factors except the mental habitus of hyperconscientiousness of ambitious type. There was an entire absence of roughness often seen in men of that occupation. In its essence the situation was that the man felt unable to, and did not want to, lead again the arduous life of a railroad man, for which he was in reality temperamentally unsuited.

But even in this case adaptation to the unpleasant environment might have been accomplished had not the pernicious influence of the struggle for indemnification preponderated so as to interfere with psychological reconstruction. Instances of this kind are numerous. Isolated examples spring to the mind of every railroad surgeon; but an extensive comparison between cases equal in value to a deliberate experiment is best afforded by the observation of a train wreck in which 200 passengers were injured, about half of them severely. Only about 20 of these passengers developed traumatic neurosis. Some of these received heavy damages, upon which their health was immediately restored. In one case, however, a cure was effected by Dr. Bevan, the observer, without recourse to a lawsuit; but even this was done against the active protestations of the patient and only by extraordinary perseverance and determination on the part of the physician, whose method of persuasion was so insistent as to make the patient weep.

COMPENSATION NOT CURATIVE. But it is not always that the indemnity effects the cure. There is a case well known in Washington where \$17,000 was allowed by the court to a man in whom a street-car accident induced the belief that he was incapable of locomotion. This lasted for seven years, during which the patient went about in a wheel-chair administered by a solicitous wife. His wife's belief that he could not walk was rudely disturbed after the plaster had fallen from the roof while they were asleep in bed one night, when she found her husband seated in the corner of the room twelve feet from the head of the bed. She argued that if he could walk while asleep at night he could walk while awake by day. This he did in trembling fear after insistent persuasion by her, and eventually recovered in a few days.

It would be idle to pretend that these were deliberate simulators for gain. They were honest pretenders, just so much as is any genuine hysterical the victim of a suggestion that he is incapacitated. These cases must be carefully differentiated from those who intentionally imitate symptoms in the hope of gain, even although the gain be merely the sympathy, attention, or notoriety from other people. The first type we call malingerers, the second mytho-

maniacs, fantasticals, or pathological liars; neither of these types has immunity from the psychological reaction of suggestibility, which may eventuate in the genuine medical hysteria.

The initiator of symptoms may, of course, be an actual accident or disease; and equally so it may be derived from the mere idea of injury or of disease, so that the clinical problem to be analyzed may be exceedingly complex. Besides this the patient may refuse access to his psychological ground work, perhaps merely on account of shyness or shame of thoughts concerning which he fears misunderstanding or ridicule, and entirely apart from any question of venality. This phenomenon is found very commonly in psychoanalytic work, and it is the shame-faced reticences of patients which have led to the need of the use by some analysis of mechanistic expedients, such as the association-experiment (Jung), the dream unravelling, and the free-flow association.

These genuine psychoneurotics are entirely curable, quite apart from any question of indemnity in itself; but the struggle for indemnity cannot be given up without loss of self-respect in the implied confession of dishonesty or at least of the gross error of psychological interpretation concerning the role of the accident itself as the provoker of the illness; so that there is a preoccupying search by the patient for facts to ratify his belief that the accident had damaged him. This inevitably leads to imaginations, exaggerations, and falsifications inevitable for a mind not scientifically trained. It is only when the patient has a glimmering of his mistake that he begins in desperation to defend it by conscious self-deception in order to bolster up a psychosocial attitude the negation of which would, he believes, be derogatory.

The construction of this state of mind is thus described in my article before the 1913 International Congress of Medicine:

"Especially prone to this damaging sequence are persons whose imagination has been made rampant by the cultivation of the credulous fears of childhood; their fear-reaction to that which they do not understand is a dominant one, and they are easily beset by an idea linked with fear. The commonest of the fears which result from accident or injury is that of bodily harm. It is difficult for a person of this type, when ignorant of his own structure and functions, to shake off the foreboding created by an impressive catastrophe; and it must not be forgotten that what others regard as trifling the victim may look upon as catastrophic, judged by its possible effect on him. Prepossession by the idea of one's own disability is an inevitable consequence. This leads to abstraction from and inattention to the affairs of ordinary life, which, if not trifling by comparison in the patient's mind at least cannot claim the attention properly needed. Hence ensues the well-known diminution of the capacity to think, work, or take part in social life. This incapacity, when the patient becomes aware of it, leads

him to still further accentuate the result of his injury and thus to augment his alarm about his health. Thus is constituted the vicious circle of hypochondria. Even a nosophobia may ensue, such as the fear of lost manhood, insanity, paralysis. Alarm at this impending disaster must, of course, be distinguished from the primary alarm due to the accident itself."

FORENSIC PRESENTABILITY. This mechanism is so simple that it can clearly be grasped by any intelligent person even without medical training; it has been very convincingly popularized by Mr. Addington Bruce in the *Outlook* of May 9, 1914. There should be no difficulty, then, in convincing a court of the nature of these cases and of their curability when properly dealt with, and this should lead to an equitable appraisalment for damages for loss of time and distress of mind. That this is not at present the case we believe to be due to the want of knowledge of many expert witnesses concerning the whole subject of the psychoneuroses. The point of view here set forth is entirely foreign to a mind of which the habit has been to be content with the farrago of confusions which was all that the older text-books afforded concerning functional nervous affections. Besides this, the appraisalment of the functional nervous affection is inextricably interwoven with the whole subject of neurological diagnosis. A physician who is not thoroughly conversant with modern neurology is sure to give the jury a false impression of the status of his case unless he strictly confines himself to concrete facts observed by himself and leaves their interpretation to the neurological expert who follows him. In the conduct of such cases counsel should entirely discard the antiquated and misleading accounts in text-books of medicine and neurology; the issue should be presented solely by concrete facts elicited from the patient himself as observed by medical men and others, and the interpretation of these aside from all technical concepts in the plane of simple good sense, which means good psychology. A striking instance of this error has just transpired in the District of Columbia, where a case carefully outlined on this basis was thrown into confusion by the introduction of a general practitioner who, without adequate knowledge, took it upon himself to instruct the jury concerning neurological and psychopathological interpretations of which his hazy knowledge was only second-hand.

It was the case of a woman who after a trifling glass cut and a knock on the elbow gradually developed a complete flaccid paralysis of the right arm. The allegation of neuritis was easily disproved; the joints were not diseased; the spinal cord was intact, and the brain centre was not damaged. These were shown by complete mobility, absence of wasting, presence of the reflexes without exaggeration or spasticity. The psychogenetic nature of the paralysis was very clear, and the patient's own physician fully admitted this in the witness-box, and also that such paralyses often occurred without trauma of the body at all. Facts of this kind

are really not difficult to demonstrate to a jury if a properly trained psychopathologist is employed.

This was demonstrated very clearly in the case of *Hill v. Chicago, Milwaukee & St. Paul Railroad*, at Redwing, Minnesota, December, 1911. Here the psychogenetic nature of an affection which simulated lameness alleged to be due to sacro-iliac and lumbar injury was so clearly shown the jury that instead of \$15,000 damages demanded the allowance given was merely \$1,500 for loss of time and stress of mind. This was a particularly "dangerous" case from the forensic aspect; but the railroad had become weary of paying indemnities for psychological accidents, and made this test case. The crucial point depended upon a demonstration by the neurologist that the attitude and movements of the patient did not conform to a syndrome which should have been present had the injury been where believed. This, along with the integrity of the reflexes and lack of wasting, convinced the jury that no lesion was present.

In conclusion, let me emphasize the importance of the fact that functional nervous syndromes which occur after accidents differ in no way from those found in persons who have been subjected to no accident at all. The accident then was a red herring across the trail of the real cause of the psychoneurosis. These doctrines have already been elaborated by me with numerous illustrations.

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GRANULOMA FUNGOIDES.¹

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(From the Pathological Laboratory of the Samaritan Hospital.)

THIS condition, first described by Alibert in 1834, is a cutaneous disease which since then has been the object of investigation by many authors. Nevertheless, the origin of the disease still remains obscure.

¹ Presented before the Pathological Society of Philadelphia, April 9, 1914.

An instance of this condition came under my study at the Samaritan Hospital. The case was kindly referred for my pathological study by Dr. Edward B. Finck, to whom I wish to express my thanks. The history of the case is as follows:

J. T., male, aged thirty-four years; white; born in the United States; occupation, steam-fitter.

Family History. The family history is negative so far as his present condition is concerned.

Personal History. He was perfectly well until twelve years ago, when he noticed the appearance of a rash, first on the trunk, and then it spread to other parts of the body. Itching was intolerable. He was under the care of various physicians without getting much relief. A year ago a few small tumors developed. About seven months ago a few large tumors appeared, involving chiefly the shoulders, trunk, and neck. At this time he came under the observation of Dr. Finck.

On examination we find the tumors situated upon the shoulders, neck, and trunk. In between these tumors there are large areas of scaly eczematoïd appearance, diffuse, and intensely itching. The tumors number from twenty to thirty, and vary in size. Some are as large as a pea, others attain the size of a large tomato, especially those which are situated upon shoulders and neck. The color of most of the tumors is bright red and some are of a dull-red color. On palpation, fluctuation is present in the greater proportion of the tumors. The lymph glands at the time of examination are not enlarged; however, the patient said upon questioning that the inguinal glands became large at times and then returned to normal size. Several of the tumors show slight ulcerations. The patient was transferred to the Polyclinic Hospital.

The blood examination was as follows:

Wassermann reaction negative: Red-blood cells, 4,960,000; white-blood cells, 20,200; hemoglobin, 62+. Differential count: small lymphocytes, 15; large lymphocytes, 4; transitionals, 2; polymorphonuclears, 81; basophiles, 0; eosinophiles, 0; color index, 0.63.

A nodule was excised from the left hypochondriac region, fixed in formalin, and embedded in colloidin. Section stained with hematoxylin and eosin, polychrome methylene blue, Mallory anilin blue, Giemsa's; a piece of tissue was likewise treated by Levaditi's method. The pathological report is as follows:

The tumor is ovoid, somewhat roundish; long diameter, 3 cm., transverse diameter, 2 cm., and of a semisolid consistency. The capsule of the tumor is somewhat thick and firm.

The microscopic picture is as follows:

In places where the infiltration is slight the papillæ are well preserved; in other areas where the infiltration is dense the papillæ are thinned and flattened out. In some places there seems to be

an infiltration with small round cells which occupy preformed spaces between the Malpighian layer and stratum lucidum. The subepithelial connective tissue seems to be masked by dense infiltrations of cells which vary greatly in their morphology. However, the bulk of the infiltrated areas is made up of small round cells poor in protoplasm; their nuclei stain intensely with the basic stains and resemble lymphocytes. Besides these small round cells there are scattered throughout the corium somewhat ovoid cells larger than the round cells; they are pale, vesicular, and show many mitotic figures. Several giant cells are also observed. The collections of cells are surrounded by loose connective tissue. In some

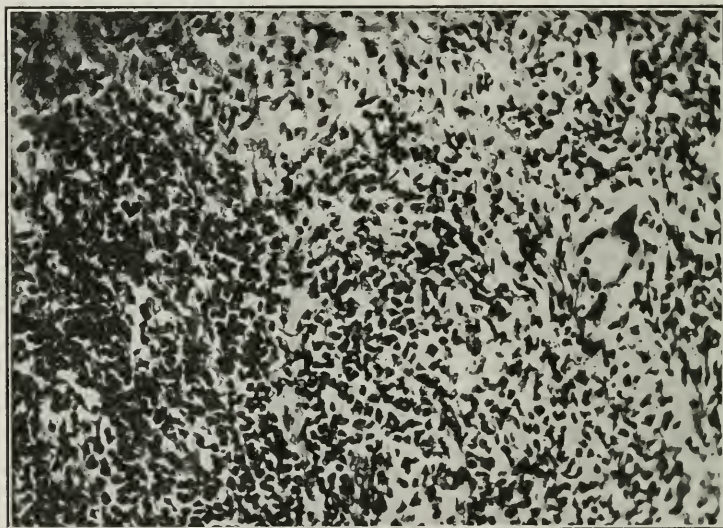


Fig. 1.—Microscopic picture of the specimen of our case. 1, note the dense cellular infiltration; 2, great variety of cells; 3, giant cell.

places the connective tissue is undergoing degeneration. Imperfectly developed capillaries are present. The majority of the capillaries are filled with round cells. Sweat glands are encircled by dense accumulations of the small round cells. The epithelial lining is undergoing proliferation.

Although Rindfleisch, Auspitz, Hammer, Vidal, and others have described microorganisms in the lymphoid tissue of cases of granuloma fungoides, yet the germ cultivated and inoculated into rabbits from a similar condition by Lassar and Doenitz did not provoke the pathological lesions characterizing granuloma fungoides. In our case the appearance of what would suggest some micrococci represents probably granules of broken-down cells. It remains for the future to determine the definite etiological factor. Yet there are some points collected from the literature which seem to have an etiological bearing upon the disease. Thus it seems to

have occurred not more than once in a family. In our case the family history is negative. Previous venereal history has been eliminated in our case by the negative Wassermann. It has occurred more in the male sex and in individuals of robust constitution and over thirty years of age. However, there was a case reported before twenty years of age. Our patient in regard to age comes within the general rule. The pathology offers a good deal of speculation and the histological picture of the lesions helps us to understand the clinical manifestations of the disease.

Granuloma fungoides occurs in two forms:

1. A form with a prefungoid stage, "érythémie mycosique" of Hallopeau and Besnier.

2. A form without a prefungoid stage, the "tumeurs d'emblée" of the French school.

The above classification is essentially in accordance with the views of Crocker, Unna, and the more modern authors.

The prefungoid stage may last for months and years. In our case it lasted for twelve years. It is characterized by a scaly or vesicular or by a dark-red, sharply circumscribed rash, or by a sort of urticaria. The dermatoses may appear and disappear several times before the tumors develop. The prefungoid stage is the most difficult to diagnose. In this stage the pathological changes are limited to the subpapillary vascular layer of the skin. Lerrede found a proliferation of fixed connective-tissue cells around the bloodvessels; likewise he observed some mast cells. Unna lays great stress upon the dilatation of blood and lymph spaces, which are prominent in this stage. This latter point stands in direct contrast to granuloma of tuberculosis and syphilis where the bloodvessels are obliterated. On account of the dilatation of the vessels in the papillæ there appears the hyperemia and edema of the skin. The edema of the skin in some cases forms a characteristic feature of the prefungoid stage. By and by the changes extend to the cutis until the hair follicles and glands disappear. This, however, occurs late. Before they are affected tumors may have formed; the epidermis becomes protruded, due to pressure occasioned by the cellular infiltration from beneath; then tumors form. They form nodules the size of a walnut or fist, and are of a bright red color. The tumors are sharply defined, more and more elevated, and then assume the appearance of tomatoes not only in their size and color but in structure, the capsule being thick and the contents semisolid.

The tumors develop on any part of the body or may be confined to the face, axillæ, or to a limb. In severe cases they may spread all over the body. In our case they are located on the shoulders, trunk, arms, and neck.

The tumors may form without a preceding erythema, "tumeurs d'emblée." In this form the number of nodules is more limited

than in the first one. The microscope shows that the tumor stage is an exaggeration of the prefungoid stage.

The tumor consists of loose connective tissue which encircles groups of cells which vary greatly in size and shape. In our case the cells as detailed above are small round cells; they are poor in protoplasm; the nuclei take an intense basic color; they are at best brought out by the polychrome methylene blue stain. These cells make up the bulk of the tumor. Some of them can be traced, penetrating the layers of the epidermis, and in one or two places in our sections they have accumulated in spaces between the Malpighian and stratum lucidum. Then one observes short spindle cells scattered in between the groups of the small round cells. The origin of the spindle cells is a matter of speculation.

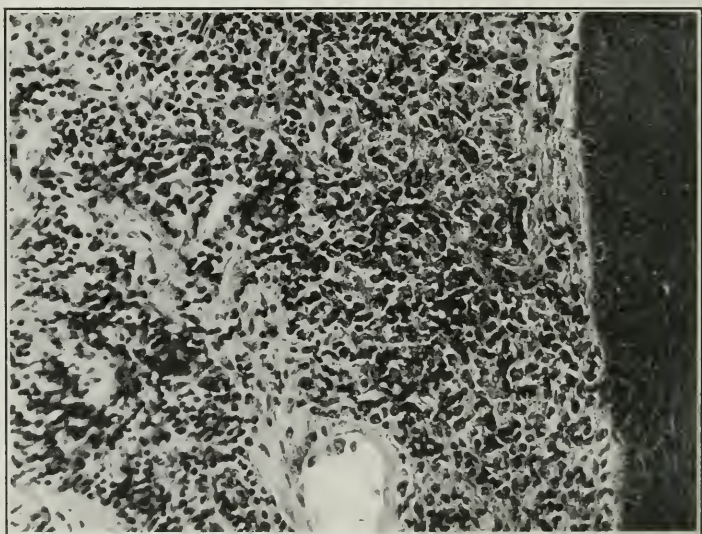


FIG. 2.—Note the flattened-out papillæ; 2, blood-spaces are filled with cells similar to those that make up the bulk of the tumor.

Cells somewhat ovoid, larger than the round cells, are noticed. The nuclei of these cells are paler than those of the small round cells; many of these cells show mitotic figures, and likewise one can see that these cells are undergoing crenation and fragmentation; what appear have rings of granules, probably the remnant of the ovoid large cells. Whether these cells correspond to the cells described by Unna as specific of granuloma fungoides we are not prepared to say.

An interesting question arises as to the source of the cells. Lerrede representing the French school, and Poltauf, the Austrian, believe that the cells are partly derived from the lymphocytes of the blood. From the study of our case we are inclined to share Unna's view-

point that the cell infiltration is derived from the connective tissue; for were the origin of the cells the blood then the blood analysis ought to show some changes, while this is not the case, as in our patient the small lymphocytes were fifteen and the large lymphocytes 4 per cent.

In our sections a few dilated bloodvessels are seen which in addition to the red cells contain cells similar to those found in the tumor. This fact would show that the tumor cells are being carried away from rather than being brought to the tissue affected. Besides the above cells we have seen one or two eosinophiles; several giant cells were also observed.

Plasma and mast cells have been reported to have occurred in cases of Galloway, Macleord, Lerrede, etc.; in our case sections stained for them did not reveal any.

The connective tissue of the subepithelial layer in our sections has become obscured by the cellular infiltraton. In some areas the connective tissue is degenerated (it stains pale pink with Giemsa's stain). The degeneration probably results from the pressure exerted by the cellular infiltration. In between the cells of the tumor one can find occasional fine fibrous threads.

In the prefungoid stage Unna claims that the elastic tissue is preserved. On account of this latter finding, Ranvier has classified the condition under cutaneous lymphadenie, the tissue resembling a lymphoid structure, yet this view-point is rejected by the more advanced work on the subject.

In our case the cells in some places go as deep as the subcutaneous fat tissue; however, they do not penetrate the underlying deep structures. Some of the hair follicles and sweat glands are embedded in a collection of small round cells, and in some places the sweat glands have undergone proliferation. The question whether the proliferation of the glandular epithelium is due to a stimulation caused by the cell infiltration or whether it is secondary to a toxin irritation can be speculated upon.

Whether there is some newly formed connective tissue or what appears to be connective tissue is merely the contrast between the displaced connective tissue by the cells and the tissue that is left is difficult to determine. It seems to us, however, that the cellular infiltration might have lodged upon the connective tissue and obscured it; and after the cells have become fragmented and absorbed then the preëxisting connective tissue came again to the front. This may explain the clinical picture of absence of scar tissue after spontaneous healing of the tumors.

The tumors may appear two or three years after the rash, or a longer interval of time may elapse. Our patient developed the tumors twelve years after the beginning of the rash. These tumors when properly treated usually do not recur, and when treated early they do not provoke any constitutional symptoms or cachexia. If allowed to go on untreated the patient usually dies from exhaus-

tion or from toxemia as a result of necrosis that takes place in the tumors. An interesting point about the tumors is that they do not give metastasis to any of the internal organs. However, cases with metastasis in the spleen have been reported. Duhring and Galliard also observed what appeared a metastatic growth in the bladder. Kaposi and Poltauf and others have reported metastatic tumors in the liver, pancreas, kidney, etc. Brandweiner has found metastatic growth in the brain. These cases are exceptional, and then it is questionable whether the metastatic tumors are of the same histological structure as the granuloma of the skin. It might be that a secondary lymphosarcoma has developed upon the site of the granuloma with the metastasis.

More commonly there is a hyperplasia of the lymphatics in various parts of the body.

Another interesting feature about these tumors is their spontaneous disappearance without leaving any trace behind them. The reason for it has been given above.

Granuloma fungoides must be differentiated from (1) sarcoma, (2) leukemia. Sarcoma arises from previously healthy skin; granuloma fungoides from a previously diseased skin. Sarcoma grows progressively in depth and involves the neighboring tissues; granuloma fungoides grows more in width and never penetrates the underlying neighboring tissues; sarcoma gives metastasis to the internal organs; granuloma fungoides rarely gives metastasis. Clinically, sarcoma runs a different course than granuloma fungoides; it does not tend to a rapid appearance and subsequent disappearance by absorption and necrosis as seen in granuloma fungoides.

Histologically: In sarcoma the cells are more uniform in size and shape and the deeper layers of the cutis are involved first and the epidermis not at all unless it breaks down. In granuloma fungoides there is a great variety of cells and the infiltration is superficial.

From leukemia it must be differentiated, for there are a great many authors, especially of the French school (Lerrede), and only recently Pellagiti, who have attempted to bring forth evidence as to granuloma fungoides being one of the manifestations of leukemia. However, the general clinical picture and blood-findings of leukemia are sufficient proof to the contrary.

In conclusion we would state, (1) granuloma (mycosis) fungoides is primarily a chronic, cutaneous disease of unknown etiology; (2) the histological picture explains the clinical manifestations of the disease, such as the erythema and edema of the skin of the prefungoid stage, the tumor formation, and the spontaneous appearance and disappearance without any scar tissue left behind them.

REVIEWS

DISEASES OF THE HEART. By JOHN COWAN, D.Sc., M.D., F.R.F.P.S., Professor of Medicine, Anderson's College Medical School. With chapters on THE ELECTROCARDIOGRAPH. By W. T. RITCHIE, M.D., F.R.C.P.; and THE OCULAR MANIFESTATIONS IN ARTERIOSCLEROSIS. By ARTHUR J. BALLANTYNE, M.D., F.R.F.P.S. Pp. 429; 3 colored plates, 196 text illustrations. Philadelphia and New York: Lea and Febiger, 1914.

THIS work is a practical treatise upon the diseases of the heart and arteries considered in the light of the recent additions to our knowledge of the pathological histology and physiology of the heart and of the facts acquired from the use of the sphygmomanometer, polygraph and electrocardiograph, and orthodiagram.

The book opens with a chapter on the pathological changes affecting the myocardium and their clinical significance. Four chapters are devoted to the etiology, pathology, symptoms, eye-ground changes and treatment of arteriosclerosis, with a discussion of the relation of nephritis and of the accepted views upon the prognostic significance of high blood-pressure and its treatment. The myogenic theory of the cardiac action is then presented, followed by a clear exposition of the method of interpreting polygraphic tracings and electrocardiograms and of the significance of the recognized pathological alterations in these graphic records. Ten chapters are devoted to the disturbances of the myocardial function including juvenile arrhythmia, extra systoles, nodal rhythm, pulsus alternans, heart-block, dilatation, paroxysmal tachycardia, auricular flutter and auricular fibrillation. The etiology, symptomatology, characteristic graphic records, prognostic significance and treatment of each of these is considered and this portion of the book is amply illustrated with tracings and case histories. The remaining thirteen chapters are devoted to acute endocarditis, chronic valvular disease and pericarditis; their etiology, symptoms, and physical signs, with especially good chapters upon prognosis and treatment.

Of the illustrations about sixty-five portray the gross and microscopic pathology of the heart and arteries while the remainder are polygraphic, electrocardiographic, and blood-pressure curves and diagrams of the cardiac murmurs.

The author presents clearly all the important recent advances

in cardiovascular pathology and physiology and the bearing of the newer clinical methods of precision upon the diagnosis, prognosis, and treatment of cardiovascular disease.

J. H. A.

ACUTE POLIOMYELITIS. By IVAN WICKMAN. Translation by DR. WM. J. A. M. MALONEY, F.R.S. Ed. Pp. 135; 12 illustrations. New York: Journal of Nervous and Mental Disease Publishing Co.

ONE of the worst epidemics of poliomyelitis or Heine-Medin's Disease in recent years was that which occurred in 1905 simultaneously in Norway and Sweden. This was fully described by the author of the present volume, Ivan Wickman. As a consequence, this work on poliomyelitis is an excellent study of this disease, both from the clinical and pathological standpoint. Unfortunately there is nothing decidedly new that can be said regarding its etiology, prophylaxis, and treatment.

T. H. W.

THE PRACTICE OF SURGERY. By JAMES G. MUMFORD, M.D., Lecturer on Surgery in Harvard University; Surgeon of Clifton Springs Hospital, etc. Second Edition. Pp. 1032; 683 illustrations. Philadelphia and London: W. B. Saunders Co., 1914.

THE title of the work describes it accurately. It is an account of the practice of surgery—as seen in one's daily work. The facts are gleaned from years of practice in hospitals, lecture-rooms, and private work. No attempt is made to cover all the phases of surgery of today. Theories and opinions not well grounded are omitted. Pathology and bacteriology are practically omitted. The minor details and fundamental steps in a surgical training are assumed as already belonging to the reader.

There is a discussion of antiseptics, sutures, needles, anesthetics, and a host of other minor surgery subjects. In other words, the book is not one for students or beginners in surgery, but for those well grounded in the fundamentals.

The arrangement of the contents is unique in a way, precedence being given to the commoner and more important subjects. The first chapter on the abdomen and the chapter on minor surgery are the best in most respects. Here the author seems to inculcate a personal element into the text. The matter of bursæ and their diseases and fractures could be handled with a little more fulness in reference to diagnosis in the first instance and treatment in the second instance.

The book contains many illustrations that are excellent and very instructive, but there are some specimen illustrations that are useless to a surgeon. Illustrations showing the ultimate appearance of a massive cancer of the neck, or of a sarcoma of the humerus, take up space that could be used to better advantage.

On the whole, the author has given us an instructive and pleasing work in its limited field. It is well written, revised, edited, and worthy of careful perusal. E. L. E.

RESEARCH STUDIES IN PSORIASIS. By JAY F. SCHAMBERG, M.D., JOHN A. KOLMER, M.D., A. I. RINGER, M.D., and G. W. RAIZISS, PH.D. Journal of Cutaneous Diseases, Including Syphilis.

IN reviewing the excellent article of Schamberg, Kohner, Ringer, and Raiziss, and acting as a critic in regard to its deductions, it is fair to state that the 140 pages contain only the preliminary findings, and the investigation is still in progress.

The research has been conducted along two distinct lines, bacteriological and metabolic. Bacteria were sought in twenty-four cases of psoriasis, and sixteen different organisms were isolated from fifty-seven cultures. All of these were classified, excepting a diplococcus, which was discovered in five of the cases. None of the organisms reproduced the disease in either man or animal, and the findings are therefore of negative value.

The protein metabolism was studied in eight psoriatic subjects. It was found that an individual with psoriasis eliminates less nitrogen in the urine than a normal person, on a corresponding diet, and that there is also a greater retention of nitrogen, even in a low nitrogenous diet. The greatest retention of nitrogen was determined in the most extensive and severe outbreaks, and apparently was somewhat proportionate to the same. A betterment was produced if the patient was given a diet low in nitrogen. If, however, the individual after the disappearance of the eruption was fed upon highly nitrogenous food the psoriatic eruption could not be reproduced.

The writers infer that psoriasis is due to an abnormal retention of nitrogen. In order that this assumption of the investigators should prove of conclusive value, it will be necessary to cause a disappearance, rather than a betterment, of the outbreak, in a considerable number of cases, by a diet low in nitrogen, and also to reproduce the disease, after the total eradication of the eruption, by the administration of highly nitrogenous food. It is to be hoped that the continuation of the investigation will prove the cause of this chronic and troublesome disease. F. C. K.

A SYNOPSIS OF MEDICAL TREATMENT. By GEORGE CHEEVER SHATTUCK, M.D., Assistant Physician to the Massachusetts General Hospital. Second edition; pp. 96. Boston: W. M. Leonard, 1914.

THIS is a small, linen-covered volume, dealing in a brief manner with the treatment of several important medical conditions. In addition it details in summary fashion the facts concerning salvarsan, neosalvarsan, and a few of the drugs used in every-day practice.

Some new material has been added and a number of minor changes made in this second edition.

The printed matter occupies but one side of the page, while the reversed one remains for purposes of note-taking. The book was primarily prepared to meet a local didactic need, and as such it finds its only real use.

We trust that in future editions completeness will not be sacrificed for brevity. T. G. S.

CANCER: THE PROBLEM OF ITS GENESIS AND TREATMENT. By W. FORBES ROSS, Late Civil Surgeon, His Majesty's Guards' Hospital, London. Pp. 261; 4 illustrations. London: Methuen & Company.

THE book is written in popular form as an exposition of the author's views in regard to the origin and treatment of cancer. He argues that the altered nuclear division leading to cancer formation is the result of deficiency of potassium in the cells. He thinks that the administration of large doses of various salts of potassium will prevent recurrence of an operated cancer, cause the regression of inoperable cancer, and cure involved lymph nodes. He associates this form of treatment with radium emanations and kataphoresis in the form of what he calls "electrical perfusion" of potassium. In a general way the construction of the book follows a logical sequence and it is printed in large type on rough paper; but the English and punctuation are extremely careless, oftentimes to the point of confusion. The style is pedantic; and needless reiteration of fairly well established facts is interspersed with undue criticism of the conservatism of the average physician and illy drawn conclusions founded on the opinionated logic of the author. The accounts of the cases are more after the style of a patent medicine testimonial than the scientific report of a case. The records of the author's observations are incomplete, his few experiments are insufficient and his deductions are poorly founded. The book is quite unconvincing to the scientific reader. H. T. K.

OPERATIVE SURGERY. By PROFESSOR V. SCHMIEDEN, Privatdozent of Surgery in the University of Berlin and ARTHUR TURNBALL, M.B., Demonstrator of Anatomy in the University of Glasgow. Second edition. Pp. 345; 435 illustrations. New York: William Wood & Co.

THE author and English editor have compiled and presented in this comparatively small volume the subject of "Operative Surgery" in a remarkably concise, adequately illustrated and altogether commendatory manner. The present second edition has undergone much revision and contains many additions, especially in the chapters dealing with the cerebellum, tongue, pharynx, bones, joints, nasal tamponade, tooth extraction and lymphadenectomies, while the chapter on the surgery of the stomach and intestines has been entirely remodelled.

Obviously the aim of the author has been to present the fundamental or classical procedures in operative surgery, to eliminate obsolete operations and to modernize the subject as far as may be consistent with brevity.

Realizing the real purpose of the book, commendation far outweighs criticism. Nevertheless, it seems to the reviewer, that in a work of this type, some time and space should be devoted to ligatures in general and particularly to the tying of knots and a consideration of appropriate needles, etc. In the chapter on gastrointestinal surgery, the German custom of employing interrupted sutures in anastomoses appears too conspicuously in the illustrations, for a method which bears the burden of untold deaths consequent upon leakage and peritonitis.

The section on "Operations on the Urogenital System" does not impress one as being so praiseworthy as other sections. Not only here, but throughout the book there is noted, in a number of instances, a disproportionate consideration as to space devoted to operations of comparative unimportance. For instance, more space is given to external urethrotomy and almost as much to phimosis operations and amputation of the penis as to prostatectomy.

B. A. T.

VACCINE AND SERUM THERAPY. By EDWIN HENRY SCHORER, B.S., M.D., D.P.H., Assistant, Rockefeller Institute, New York City, etc. Second edition. Pp. 300; 18 illustrations, 3 charts, and 1 plate. St. Louis: C. V. Mosby Company.

THIS book gives in compact form the information useful to the general practitioner on the theory of immunity, specific diagnosis of infectious diseases, and serum and vaccine treatment. The

author makes a special point of the collaboration of specific and general methods in the diagnosis and treatment of infectious diseases. He insists on the importance of accurate diagnosis of the etiological factor, and rightly condemns empirical and "shotgun" treatment by commercial vaccines. Stress is also laid upon the superiority of autogenous over stock vaccines where the former are available.

The book should prove a useful source of information to the general practitioner upon a subject that is daily gaining more and more attention.

R. H. I.

DISEASES OF THE MOUTH, FOR PHYSICIANS, DENTISTS, MEDICAL AND DENTAL STUDENTS. By Prof. DR. F. ZINSSER, Director of the Department of Dermatology at the City Hospital, Lindenburg; Dozent at the Academy for Practical Medicine, Cologne. Translated and edited by JOHN BETHUNE STEIN, M.D., Professor of Physiology at the New York College of Dentistry, Late Instructor in Genito-urinary Diseases at the College of Physicians and Surgeons, New York City. Pp. 269; 73 illustrations. New York: Rebman Co.

UNDER this comprehensive title, the author offers us an excellent presentation of syphilis of the mouth and neighboring parts, with the differential diagnosis from conditions closely resembling that disease. In fact, the book is simply a treatise on syphilis as seen in the oral cavity, with mention of other diseases only so far as they are liable to be confused with it. There are but 67 pages of actual text, the remainder being occupied by the plates and the descriptions attached to them. The volume is therefore a hand-atlas rather than a text-book, as might be thought from the title. The plates are beautifully colored, and give life-size representations of almost all the conceivable lesions of syphilis in its various stages as it may occur in the mouth. These illustrations fulfill their purpose almost as well as actual study of the living subject.

The claim that nearly all developmental defects in the structure of the teeth are due to hereditary syphilis is contrary to general experience. The author states that rickets and tuberculosis may possibly play a part in dental hypoplasia, but makes no mention of such well recognized causes as scarlet fever and measles. The chronological chart of the calcification of the teeth given at the end of the book seems to bear out the contention that syphilis is practically the only disease that could have such a deleterious effect at the calcification period. But this period, instead of occupying only a few months after birth as claimed by the writer, in reality extends over several years for not only the crowns of the

incisors but of all the permanent teeth except the first molar. Thus the child may be exposed to the effects of several of the eruptive fevers during the calcification of the teeth, these effects showing themselves in hypoplasia.

The points to which attention has been called in no way lessen the immense value of the illustrations, for which the book is to be recommended as a great help in diagnosis. R. H. I.

MEDICAL AND SURGICAL REPORTS OF THE EPISCOPAL HOSPITAL.

Edited by A. P. C. ASHHURST, M.D. Volume II; pp. 427. Philadelphia: Wm. J. Dornan, 1914.

THE appearance of a second volume of these reports, coming so rapidly after the first, is a splendid indication of the literary activities of the Hospital Staff. The present volume maintains the same form and general characteristics as the first. It is carefully edited and contains a mass of interesting and diverse information. J. H. M., JR.

THE INTERPRETATION OF RADIUM, BEING THE SUBSTANCE OF SIX FREE POPULAR EXPERIMENTAL LECTURES DELIVERED AT THE UNIVERSITY OF GLASGO. By FREDERICK SODDY, M.A., F.R.S., Independent Lecturer in Physical Chemistry and Radioactivity in the University of Glasco. Third edition. Pp. 284, 33 illustrations. New York: G. P. Putnam's Sons.

THE work is exceedingly well written, in an interesting and popular style and, with a very few exceptions, without the use of mathematical equations. The author confines himself to the physical and chemical sides of radioactivity and does not mention the biological and therapeutic sides, except in a few sentences.

Chapter I is an introduction containing general statements in regard to the science of radioactivity. In Chapter II the author tells of the discovery of radium, and of its general properties including the evolution of energy. The next two chapters treat of the characteristics of the rays from radium; and Chapter V of the source of the energy, the atomic disintegration theory, etc. In the remaining seven chapters the relation of helium to the radioactive processes, the laws of radioactive changes, the ancestry of radium (uranium, ionium, etc.) are described; radium's descendants and their characteristics, some general ideas as to the evolutions of matter, etc., and finally, the thorium and actinium series are described. The last chapter was added for this third edition.

The character of the research work that the author has done is an ample guarantee for the general accuracy of the statements contained in the book. A few flights of fancy in Chapter V may be pardoned on the ground that they were designed to appeal to the imagination and stimulate the interest of the public. W. D.

TUBERCULIN IN DIAGNOSIS AND TREATMENT. By LOUIS HAMMAN, M.D., Associate in Medicine in the Johns Hopkins University and to the Johns Hopkins Hospital and SAMUEL WOLMAN, M.D., Instructor in Medicine in the Johns Hopkins University. Pp. 381; 30 illustrations. New York and London: D. Appleton & Co.

DURING the twenty-three years which have elapsed since Koch introduced tuberculin as a therapeutic and diagnostic agent, an enormous literature has grown on the subject, a large part of it being in foreign languages; this has been still further increased by the various diagnostic modifications. In reviewing this mass of material and bringing together what is best in a consecutive narrative, Hamman and Wolman have rendered a valuable service.

The first chapter deals with the tuberculin reaction, tuberculin hypersensitiveness, and immunity. The second chapter gives in detail the different methods of employing tuberculin for diagnostic purposes. This chapter can be read with profit by many who have hazy notions as to how the reactions are to be interpreted. This is especially true of the von Pirquet test, which is so generally employed. Of this test they say, "that a positive reaction is of considerable value in diagnosis during the first year of life, of less during the second year, of little in childhood, and none in adult life. On the other hand, a negative reaction excludes, with definite exceptions, the presence of an active tuberculous lesion." In other words, "tuberculin is an index of tuberculous infection, not of tuberculous disease—." Given a combination of obvious physical signs and definite symptoms, the use of tuberculin is not necessary. "Tuberculin can add so little to their assurance that its use, under such conditions, is superfluous."

While the authors recognize that accidents have followed the conjunctival test, they feel justified in continuing its use because their own experience has been free from untoward results. In spite of this, however, we cannot but feel that the conjunctival test should be avoided.

The third chapter considers in detail the therapeutic uses of tuberculin. Any one wishing to employ the remedy will find here an excellent account of how it should be administered.

Hamman and Wolman are of those who believe that tuberculin

has established itself. While this is true of some forms of tuberculosis, notably that involving the eye, we cannot escape the conviction that so far as pulmonary tuberculosis is concerned, a verdict "not proven" is not amiss.

H. R. M. L.

AN INTERNATIONAL SYSTEM OF OPHTHALMIC PRACTICE. Edited by WALTER L. PYLE, A.M., M.D., Philadelphia. Ophthalmic Semiology and Diagnosis by CHARLES H. BEARD, M.D., Surgeon to the Illinois Charitable Eye and Ear Infirmary (Eye Department), Oculist to the Passavant Memorial Hospital and the North Star Dispensary (Chicago). Pp. 400; 84 illustrations. Philadelphia: P. Blakiston's Son & Co.

H. R. M. L.

THIS work offers as nearly as may be to the student a guide in the diagnosis of diseases of the eye from a master of clinical ophthalmology. The author properly describes it as the only work devoted exclusively to ocular semiology. The writer does not merely detail the different symptoms, but connects them with the underlying pathological and anatomical conditions.

Unlike most systematic treatises on ophthalmology which are usually briefest in describing the diseases of the fundus, in this work the latter occupies just about one-half of the whole, a circumstance indeed to be expected from so skilful a delineator as the author who has devoted much time during the past thirty years to the original drawings from which the illustrations are derived.

Both the student and the accomplished practitioner of ophthalmology will find in this book a storehouse of most valuable information brought together in accessible form which will spare many hours search and provide him with a vade mecum to which he can constantly turn with a confidence in his daily professional labors.

T. B. S.

A TREATISE ON PELLAGRA FOR THE GENERAL PRACTITIONER. By EDWARD JENNER WOOD, S.B., M.D., Chairman of the Pellagra Commission. North Carolina Board of Health. Pp. 377; 38 illustrations. New York and London: D. Appleton & Co.

THE appearance of a new book on Pellagra seems to surfeit the field of literature on this subject, as a host of articles have recently appeared in the current magazine literature, several other treatises have just been published, and numerous boards of health have issued comprehensive and complete reports upon pellagra. However, Wood, shortly after the conception of the present work,

at a time when there was not a single complete treatise on pellagra, was taken sick and the publication of the work was delayed more than a year, during which time the subject received much attention.

Wood, after a complete historical sketch, details fully the various theories of the causation of pellagra, the most important, most widely discussed and investigated problems of the disease. The two most generally accepted theories of the cause of the disease are that it is due to a specific parasite which is possibly conveyed by an intermediary host or it is the result of the ingestion of mouldy corn which causes pellagra, either because it is an insufficient or inappropriate food, or because it contains some toxic substance or because it is a carrier of some form of parasite. The author believes that the first theory is the most acceptable and advances good arguments to uphold his position. As to the specific biting fly of the genus *Simulium* acting as the intermediate host, he does not feel so confident. In the succeeding chapters the other aspects of the disease are dealt with in a comprehensive and complete manner. The whole subject is presented in a thoroughly instructive yet most pleasing way, so that the work will stand in the forefront of American treatises on this very interesting condition.

J. H. M., JR.

TROPENKRANKHEITEN UND TROPENHYGIENE. By PROF. DR. REINHOLD RUGE, Marine-Generalarzt in Kiel, und DR. MAX ZUR VERTH, Marine Oberstabsarzt in Kiel. Pp. 463; 201 illustrations; 8 maps. Leipzig: Klinkhardt.

THE authors open with a discussion of tropical climates, acclimatization, clothing, habitation, diet, and other general considerations in relation to residence in the tropics. They then proceed to take up with great thoroughness the discussion of specific diseases. Distribution is considered at length for each disease and is illustrated by shaded maps for malaria, sleeping sickness, kala-azar, yellow fever, beri beri, schistosomiasis, ankylostomiasis, and filariasis. The life history of the etiologic organism of each disease receives liberal consideration. The pathology, symptomatology and treatment follow.

The infectious diseases and the infestations with worms or arthropods are first considered. Then tropical skin diseases, from various animal and plant venoms or poisons, and finally a brief discussion of the peculiarities of the universally distributed diseases when occurring in the tropics. The book is liberally provided with illustrations of lesions, of etiologic organisms, and of temperature charts.

J. H. A.

HOW TO DIAGNOSE SMALLPOX. By W. McC. WANKLYN, B.A. (Cantab.), M.R.C.S., L.R.C.P., D.P.H., Assistant Medical Officer of the London County Council, and Formerly Medical Superintendent of the River Ambulance Service (Smallpox) of the Metropolitan Asylums Board. Pp. 104; 11 illustrations. New York: Paul B. Hoeber, 1914.

THE writer has compiled a practical volume, with charts and a few excellent photographs, to assist in the diagnosis of smallpox, both in its common and rare forms. The usual distribution of the typical outbreak is emphasized; the rash is observed in ascending order of density on the abdomen, chest, back, arms, legs, and face; the outbreak showing a great predilection for the exposed portions of the body and areas of irritation.

The subject is treated in eleven chapters. The spread of smallpox by unrecognized cases; unrecognized cases and their remedy; practical points in the method of examination; individual cases of smallpox considered with a view of diagnosis; individual cases and other features of the rash; explanation of the distribution of the rash; other factors in diagnosis; differential diagnosis; initial rashes; differential diagnosis of chicken-pox and measles; additional points.

The writer comments upon the delay in the recognition of smallpox as an important factor in its spread. The important point is emphasized that the clinical recognition of the rash and its differentiation from the various exanthemata and other cutaneous outbreaks is frequently of more importance than the indefinite and frequently confusing prodromal symptoms and history. The volume is written, in a great part, in a conversational manner, making easy reading and bringing out clearly the points the writer wishes to emphasize.

The author's experience with smallpox extends over twenty years and a study of over ten thousand cases. F. C. K.

CHEMICAL PATHOLOGY. BEING A DISCUSSION OF GENERAL PATHOLOGY FROM THE STAND-POINT OF THE CHEMICAL PROCESSES INVOLVED. By H. GIDEON WELLS, PH.D., M.D., Professor of Pathology in the University of Chicago, and in Rush Medical College, Chicago. Second Edition. Pp. 616. Philadelphia and London: W. B. Saunders Co., 1914.

THE many recent substantial contributions to the literature of biological chemistry have made necessary this new edition of the standard American text-book on chemical pathology. Comparison with the original edition, published seven years ago, shows the dimensions of the book to be considerably enlarged and sixty-seven

new pages added. Especially the chapters on immunity, tumors, and diabetes are amplified. In the introductory chapters Wells gives an epitome of the modern views concerning the chemistry and physics of the cell, including in this a rather illuminating discussion on colloids, and concerning the nature and action of enzymes. Then, after covering in the next 130 pages the chemistry of bacteria, of animal parasites, and of the immunity reactions, he enters into a discussion, from a physicochemical view-point, of general pathological lesions, devoting chapters to inflammation, circulatory disturbances, edema, retrogressive changes, pigmentations, tumors, metabolic disturbances, ductless glands, and finally diabetes. To those familiar with the literature of the past decade bearing on the subjects discussed this book will be a review of the important facts established. To those who have not had the opportunity of covering that literature it will be a fascinating and able summary of the same. To all, because of the more than a thousand reference footnotes, including cross references to many other bibliographies; it will be a most valuable guide to the original sources in the literature on chemical pathology.

T. G. M.

A HANDBOOK FOR THE POSTMORTEM ROOM. By ALEXANDER G. GIBSON, D.M. (Oxon.) F.R.C.P. (Lond.), University Demonstrator in Pathology, Oxford; Honorary Assistant Pathologist to the Radcliffe Infirmary, Oxford. Pp. 136. Oxford University Press, 1914.

THIS booklet is a guide for the student in the technique of autopsies, and is based upon Virchow's methods. A large amount of anatomy is necessarily described. Lymph "glands" are mentioned instead of lymph nodes. The thoracic portion of the spinal cord should not be referred to as the "dorsal." The corpus callosum does not have "fornices." The squamous portion of the "petrous" bone doubtless means the squamous portion of the temporal bone.

As to the postmortem technique, the very practical method of measuring the body by a permanent scale, notched in the table, is not mentioned, but the old wooden staff is referred to. Examination by bacteriological methods should be at least referred to before the organs are removed, since the chapter which covers this is at the back of the book, thus minimizing the prominence and importance of such investigation. In the histological methods, in place of "4 per cent. formaldehyde" we presume 4 per cent. formalin is meant. Again, in investigation of the labyrinth of the ear, we consider the parts too minute for efficient gross inspection, and think that histological methods should be recommended instead. Englishisms should be avoided. For example, not many patholo-

gists outside of England or its colonies know the exact size of the proverbial "threepenny bit," and while most of us have seen a lung sink in water, but few have seen it "swim," yet we all have seen it float.

The book is well printed on good paper, has a flexible binding, and is of hip-pocket size. It can be warmly recommended, for a mastery of its terse directions will surely make one expert in post-mortem technique.

P. G. S., JR.

TEN SEX TALKS TO GIRLS (FOURTEEN YEARS AND OLDER). By IRVING DAVID STEINHARDT, M.D., Instructor in Clinical Surgery and Assistant Surgeon, Cornell University Medical School. Pp. 193; 6 illustrations. Philadelphia and London: J. B. Lippincott Company, 1914.

THE originals of these lectures or talks to girls were delivered before several organizations in New York, and later published in the *New York Medical Journal*. The interest in them was so great, and the demands for reprints so numerous that the author issued them with minor revisions and enlargements in their present form. The descriptions and discussions are so simple, direct, and accurate without going into unnecessary and gruesome details that physicians may well recommend the book to those seeking advice on this subject. The book would find its best use in the hands of young girls after some general instruction by mothers.

F. H. K.

FUNDAMENTAL BASIS OF NUTRITION. By GRAHAM LUSK, Professor of Physiology, Cornell University Medical College, and Scientific Director of the Russell Sage Institute of Pathology. Pp. 62. New York: Yale University Press, 1914.

IN order that those desirous of learning may obtain a better conception of the principles of nutrition than has heretofore been afforded them by the numerous popular newspaper and magazine articles that from time to time have appeared, the well-known lecture of Professor Lusk, which was delivered in 1913 as the Anniversary Address of the New York Academy of Medicine, has been published as a small book.

The subject is discussed in a way that makes it clear to any intelligent person. Facts which under ordinary circumstances would make but dry reading are presented with that resourcefulness and interest so characteristic of the distinguished author. The history of the development of our modern conception of nutrition;

the caloric needs of the body under various conditions and the importance of basing a dietary upon caloric values; the role of the various proteins in the animal economy; the dietetic habits of different races and different classes of individuals; the importance of vitamins as illustrated in beriberi; and finally the economic value of various kinds of food are discussed. No one, whether layman or physician, can read this lecture without obtaining a clearer conception of the science of nutrition and without having his attention directed to the great problems of fundamental economic importance that have arisen from our present-day dietetic habits. G. M. P.

BEDSIDE HEMATOLOGY. By GORDON R. WARD, M.D., Fellow of the Royal Society of Medicine, London. Pp. 394. Philadelphia and London: W. B. Saunders Co., 1914.

DR. WARD states that his book is intended as "an introduction to the clinical study of the so-called blood-diseases and of allied disorders." He has carefully followed this idea, so that throughout the book there is a decided tendency to stick solely to the elementary and to avoid the complicated, unproved, and much-discussed theories that are generally agitating hematologists.

The book begins with a novel classification of blood-disorders which is certainly practical. In the succeeding chapters this classification is adhered to and the various disorders in each group are fully discussed, particular stress being laid upon pathology and symptomatology. The remaining chapters deal with methods of treatment.

Several criticisms may be made of the author's method of dealing with his subject. The chapter on methods of making a blood-diagnosis is not sufficiently complete; the important blood-disorders are dismissed with too short a discussion of pathogenesis, while the less important conditions are not discussed at all from this point of view; there is an absence of good colored plates illustrative of the blood-picture in any blood-disorders; while lastly, treatment is often insufficient, while it is certainly not specific enough in most instances. The pathological sections and those dealing with the symptomatology are excellent and could be improved upon with difficulty. Furthermore, the chapter upon the blood in various diseases is particularly valuable.

The whole book is extremely practical and good common-sense is used in the handling of the subject matter. For this reason it should undoubtedly meet with a most gratifying reception.

J. H. M., JR.

DIET LISTS OF THE PRESBYTERIAN HOSPITAL, NEW YORK CITY. Compiled, with Notes, by HERBERT S. CARTER, A.M., M.D., Associate in Medicine at Columbia University and Associate Visiting Physician to the Presbyterian Hospital, New York City. Pp. 129. Philadelphia and London: W. B. Saunders Company, 1913.

THIS book in no sense is to be regarded as a work on dietetics. It is what it is represented to be, an intelligent compilation of the various diet lists that by experience at the Presbyterian Hospital have been found useful and practical.

Various types of diets are detailed in tabulated form. For example, regular house diet, convalescent diet, soft diet, milk and liquid diets are presented and briefly discussed. Various kinds of typhoid diets are next given. Salt-poor and purin-free diet lists are explained. Gastric diets are entered into with considerable care and diabetic diets are emphasized in great detail. In addition, diets for constipation, diarrhea, obesity, etc., are given. Useful features of the book are the additions of various gastric and intestinal test diets, a table of carbohydrate equivalents, and a list of useful receipts for special dishes suitable to diabetics. At the end of the book are given a table of the average chemical composition of American foods and Fisher's table of standard portions.

Frequent comments by the author furnishes valuable explanations and suggestions. For the practising physician who has little time and usually less inclination to work out accurate diet lists, this collection of diets will prove of great help and undoubted value.

G. M. P.

PHARMACOLOGY, CLINICAL AND EXPERIMENTAL. A GROUNDWORK OF MEDICAL TREATMENT. By H. H. MEYER AND R. GOTTLIEB, Professors of Pharmacology at Vienna and Heidelberg; Translated by J. T. HALSEY, Professor of Pharmacology, Therapeutics, and Clinical Medicine at Tulane University. Pp. 604; 64 illustrations. Philadelphia and London: J. B. Lippincott & Co., 1914.

CONSIDERING pharmacology as the "reaction of living organisms to various chemical agents," the authors have made an able presentation of scientific drug therapy, with frequent references to physiology and the seat and causes of the pathological conditions involved. As its name implies, their book is more than a text-book of therapeutics, in that it considers the pharmacological action of certain drugs not used in medicine, for example, curare, the first drug discussed. On the other hand, it does not attempt to include remedies other than drugs, such as massage, electricity, baths and so forth.

A fundamental division of all drugs is made into two classes: Organotropic (drugs influencing organs and their functions), and etiotropic (those acting on the causative agents of disease). The table of contents is divided into eighteen chapters, the first fourteen being devoted to the pharmacology of the several organs; the last four to the pharmacology of heat regulation, of inflammation, etiological pharmacological agents, and factors influencing pharmacological reactions. Drugs are not considered individually, but under each organ that they affect pharmacologically. A copious list of original sources is given at the end of each chapter. All doses are given in the metric system only.

Numerous additional facts and opinions are inserted by the translator. These so frequently disagree with the authors and sometimes supply such serious omissions, that an original work by the translator would be awaited with interest. For example the important effect of digitalis on the conductivity of the heart, so well demonstrated, by Cushny, Mackenzie, and Lewis, is briefly dealt with between brackets on page 266.

The subject matter appears on the whole to be accurately and adequately given. Many of the newer synthetic compounds are given, with cautious estimations as to their probable value. Among the cathartics, the phthaleins are emphasized, including the phenol-tetrachlorophthalein advocated by Abel and Rowntree. One is surprised, however, to find no mention of agar-agar or liquid petrolatum among the laxatives.

The book is well bound and well printed on good paper. A dangerous slip occurs on page 38, where 0.02 gm. of pantopon is said to correspond to 0.1 gm. of morphin instead of 0.01 gm. of morphin.

E. B. K.

THE CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL, CHICAGO. Vol. III, No. 2, April, 1914. Pp. 212; 58 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

THE April number of Murphy's *Clinics* contains the first of "Murphy's Clinical Talks on Surgical and General Diagnosis," which have been advertised as a new feature for the current year. This talk has special reference to empyema, and to the Abderhalden test in tubal pregnancy. In the case of empyema presented the treatment consisted in drainage of the pleural cavity by a rubber tube inserted through an intercostal incision. There follow three cases of ectopia testis; a case of cholelithiasis treated by cholecystectomy; and a case of "acute pancreatic cyst." The latter was recognized eventually as a case of carcinoma, with pancreatogastric fistula; but its origin, whether gastric or pancreatic, does not appear to have been determined.

Dr. Mix continues to contribute the main interest to the discussion of "borderline" cases by his able presentation of facts bearing on diagnosis. Sometimes, however, it seems that the audience becomes confused by these discussions. Thus at page 274, during an operation on a patient with duodenal ulcer, Dr. Murphy says, "The air in the stomach has gone into the jejunum, and the stomach is collapsed." A visiting doctor remarks, "Dr. Mix just made the statement that there was gas in the stomach;" to which Dr. Mix rejoins: "No, I said that there was no gas in the stomach. I said that persons with duodenal ulcer frequently complained of gas in the stomach, and that it was not gas in the stomach but air pumped there in order to get rid of gas." Evidently the visitor did not appreciate the nice distinction between air and gas.

The classification of pathological conditions encountered in the thyroid gland, given by Dr. Murphy, is one that should be memorized by every general practitioner; it is only two pages long.

The most valuable portion of the present number is that on tuberculosis of the kidney, although here again classification and operative statistics from foreign clinics occupy a space of two pages. But Dr. Murphy has assembled the case histories of three patients recently operated upon, though at different times, and presents a clinical discussion of symptomatology and diagnosis which is as good as anything that has yet appeared in the *Clinics*.

Several cases of nerve lesions conclude the volume. In one of these patients, who suffered with pain referred to an amputated leg, sections of the sciatic nerve had been removed on various occasions by different surgeons, and he was at last sent to Dr. Murphy with the suggestion that the pain might be "cortical" in origin. Dr. Murphy and Dr. Mix reached the conclusion that it was neither cortical nor due to amputation neuromata, but to an ascending neuritis; and Dr. Murphy divided half of the cauda equina, which was found red and apparently inflamed. There was much immediate relief of pain, but in a few weeks the patient claimed that there was a return of the same pain, and Dr. Murphy concluded that in the light of our present knowledge of sensory nerve-root phenomena, such a recurrence of pain was inexplicable. The question arises, Was the pain really only psychological?

A. P. C. A.

THE CLINICS OF JOHN B. MURPHY, M.D., AT MERCY HOSPITAL,
CHICAGO. Vol. III, No. 3, June, 1914. Pp. 207; 55 illustrations.
Philadelphia and London: W. B. Saunders Company, 1914.

THIS remarkable periodical is constantly springing new surprises on its readers. Here on the first page of the present number

is inserted a note to Dr. Murphy from the President of the senior class of the Northwestern University Medical School, expressing the thanks of the class to Dr. Murphy and his staff for their "regularity, punctuality, and faithful and efficient service in giving to us such a thorough and systematic course of instruction as we have received during this past school year." Next comes a remark by a "Gentleman" (in caps. and small caps.): "What's the matter with him?" The Class: "He's all right." Then follow Dr. Murphy's remarks in appreciation of the class' action.

Now, who, we may ask, is responsible for the insertion of this vulgar clap-trap? Is it the editor himself or is it the publisher? Is this kind of thing going to be continued, or is *Murphy's Clinics* ever to become a self-contained, dignified, non-notoriety seeking medium of conveying surgical knowledge? There are so many excellent features about these *Clinics* that it makes one sick at his stomach to find every once in a while such assaults as these on his sense of propriety.

One excellent feature in the present number is the discussion on the differential diagnosis of gastric and duodenal ulcer by Dr. Murphy and Dr. Charles L. Mix. There are also a number of case reports of tenoplasty, tendon transplantation, neuroplasty, etc., for deformities and disabilities of the hands and feet following infantile paralysis, traumatisms, infections, etc.; a case of arthroplasty of the elbow with a "splendid" result, although only 45 degrees of motion was present after five weeks; and several operations for fractures. There is also recorded a case of carcinoma of the hip, metastatic from the breast, treated by excision of the hip, and, at a subsequent operation, by bone transplantation to fill the defect. The patient had no recurrence, and was walking around the hospital, with the aid of crutches, when last reported, three months after operation. This is an example of Dr. Murphy's pioneer work. It makes conservative surgeons hold their breath and wait to see what is going to happen next.

A. P. C. A.

COLLECTED PAPERS BY THE STAFF OF ST. MARY'S HOSPITAL, MAYO CLINIC, ROCHESTER, MINNESOTA, 1913. Edited by Mrs. M. H. MELLISH. Pp. 819; 335 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

No fewer than twenty-eight names appear in the list of contributors to this year's volume from the Mayo clinic, and about a dozen of the names are unfamiliar, showing that "new blood" is constantly being infused into the work.

The papers dealing with the alimentary canal continue to hold first place in order of presentation and in quantity, but other departments of surgery seem to be eager contestants for the latter honor.

Second in order of presentation comes the department of urino-genital organs, which has advanced to its present highly honorable title from the less fashionable term genito-urinary (1905-1911), through that of urogenital, employed in the volume for 1912. May we expect next year to see it appear under the still more aristocratic title of urology? Third in order are the papers on the surgery of the ductless glands, all of them this year dealing with the thyroid gland. There follow eleven articles dealing with the surgery of the head, trunk, and extremities; eight on "technique;" and five general papers not otherwise classified, among them an interesting account of a visit paid by Dr. W. J. Mayo to some of the most important surgical clinics of Germany, Belgium, and Great Britain.

These articles, covering such a wide range of subjects, naturally are of various importance. Some are so excellent that others suffer by comparison. Were the latter found in the average medical weekly they probably would pass muster, but several of them are unworthy of preservation in a bound volume. It is not that the subjects of these inferior contributions are not of importance, not that they are not well presented, but that having been read once before some small country or suburban medical society, the address has then and there served its purpose when it has been delivered orally; it contains no record of new facts, reports no case histories, and being merely an ephemeral production has no justification for attempts at immortality. In a few instances the offence is carried further, and two or more papers of this description on closely allied if not indeed identical subjects are produced side by side, under the name of the same author. This criticism, which appears to us to be just, applies not only to the present volume but to past volumes as well; occurring only once it might be overlooked, but a persistent fault requires correction.

The contributions which appear to have most to recommend them are a few among those in the section dealing with the alimentary tract, such as Graham's observations on peptic ulcers; Smithie's on gastric ulcer and gastric cancer; and Carman on the Röntgen rays in gastric cancer and ulcer; as well as a series of papers on the surgery of the female breast. It is curious to see the emphasis placed on ether as the best general anesthetic under all circumstances, and amusing to read the contemptuous remarks about nitrous oxide and oxygen anesthesia, since such contempt surely argues inexperience of satisfactory administration and of its resultant advantages.

It is a pity that the table of contents does not include the authors' names. The index of contributors, at p. 789, does not supply this deficiency. And it would give a certain added authority to the opinions expressed if somewhere the official status of the writers were described. A few other questions arise: Why is the cumbrous term "intercarotid paraganglion" better than our old friend the carotid body? Is the "new motor meal" described at p. 715

designed for automobile parties? Is not Mr. Thompson Walker intended at p. 761 when reference is made to Mr. Thomas Walker? And in the same place why is Mr. Burghard's name so misspelled?
A. P. C. A.

SURGERY OF THE VASCULAR SYSTEM. By BERTRAM M. BERNHEIM, A.B., M.D., Instructor in Surgery, Johns Hopkins University, Baltimore, Md. Pp. 104; 53 illustrations. Philadelphia and London: J. B. Lippincott Company.

BERNHEIM gives in sufficient detail, and with excellent illustrations, accounts of the methods of transfusion, bloodvessel suture, transplantation of a segment of vein or artery, and arteriovenous anastomosis or reversal of the circulation. The sections which follow evidently have been included only in an attempt to justify the sounding title which is given to this little monograph. These sections (varicose veins, surgery of the heart, aneurysms) are discussed in an entirely inadequate manner, even as regards questions of mere technique. The volume is padded, moreover, by twenty pages of statistics of operations for aneurysm abstracted from the classical articles of Monod and Vanverts. In view of the evident desire to issue a volume of fair size it is inexplicable that Bernheim should have omitted the terminal S in the name of the latter author.

In a new edition we believe it will be well for the author to eliminate some of the preaching in the earlier chapters and to limit the later chapters to descriptions of technique.

A. P. C. A.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Hematuria in Appendicitis.—CARLIER and LEROY (*Progr. Méd.*, 1914, xxvii, 102) deal with the occurrence of hematuria during the course of appendicitis and independent of any lesion in the genito-urinary tract. This condition has received considerable attention in recent time and has been observed in both acute and chronic forms of appendicitis. In chronic cases hematuria may be the first and only symptom occurring suddenly in apparently normal individuals following a strain, sudden exposure to cold, etc. The hematuria may occur without pain, or may be accompanied by pain simulating renal colic. It may last only during micturition, occur every day, or recur at infrequent intervals over a period of years. Only after an exploratory laparotomy is the inflamed condition of the appendix discovered, and after its removal the hematuria permanently ceases. The same symptoms may occur during the course of an acute case, and if anything, are more prominent here. By suitable examination it has been shown that the bleeding comes quite consistently from the right side. In an analysis of 14 cases it was found in 9 that the tissues about the ureter were involved in the inflammatory process, but apparently injury to the urethral mucosa was not the cause for the hemorrhage. The bleeding might be explained on the basis of a nephritis induced by toxins originating in the appendix, but the occurrence of the right-sided source of the bleeding points to a closer relationship, which is explained by Carlier and Leroy on the assumption that either sterile or infected emboli reach the kidney by way of the retro-peritoneal veins and cause three infarctions or very circumscribed inflammation resulting in the former case in a simple hematuria, or in the latter a moderate grade of nephritis of the acute type.

A Rapid Clinical Test for Hyperglycemia.—GITLOW and HOROWITZ (*Biochem. Bull.*, 1914, iii, 272) have attempted to devise a rapid clinical method for the detection of hyperglycemia, especially one which can be applied to very small quantities of blood and one that is as useful to the practicing physician as the Fehling's reaction. The reagents employed are sulfuric acid, water, alpha-naphthol and alcohol, as used in the test originally devised by Molisch. The reagents are best added in the following order: alpha-naphthol; the solution to be tested; water and sulfuric acid; the latter two must be in the same amounts in all the tests. It is possible that a modification of this method which is not described in detail in the present paper may be applied to quantitative examination of sugar in the blood. Gitlow and Horowitz feel that the test is excellent and that the difference in color between tests performed on normal and hyperglycemic bloods is very marked and very readily detected.

The Origin and Development of Crescents.—THOMSON (*Annals Trop. Med. and Par.*, 1914, viii, 85) deals with a study of crescents made on living individuals and in autopsy smears from cases dying in the Panama Canal Zone. The general deductions as the result of the observations made may be summarized as follows: Crescents require about ten days for their development into the adult state. This development takes place chiefly in the bone marrow and spleen. During all stages of its development the protoplasm of the crescent stains a greenish-blue and often a yellow color as compared with the deeper blue of the asexual schizonts. On the other hand the chromatin stains more faintly than in the latter, is less abundant and more granular and never breaks up into masses such as are seen in the segmenting forms. As regards the pigment in developing crescents, this appears very early and remains scattered until the adult stage is reached. Thomson was able to find adult crescents in autopsy smears in spleen and bone marrow after eleven days' treatment with quinin. No evidence was obtained of parthenogenesis in crescents. From observations made upon crescents found in the peripheral blood the following conclusions are drawn: (1) Crescents are produced from ordinary asexual spores which develop somewhere in the internal organs and appear suddenly in the peripheral blood. The period of development is about ten days and the period of life in the circulating blood not more than a few days. The occurrence of crescents in the peripheral blood over long periods of time is due to the fact that they are constantly being replenished from recent asexual forms. Fresh broods of crescents appear in the blood every day, every other day, or at irregular intervals, depending upon the asexual sporulation. It would seem that quinin has no direct destructive action upon crescents either during their development or after, but it destroys the asexual spores, the source of supply. Further observations tend to show that crescents tend to become spherical in about four minutes after the blood is drawn. This appeared to coincide with the time of blood coagulation. This spherulation is probably the result of osmotic changes and this in turn stimulates flagellation. There is no evidence, however, to support the idea that crescents ever flagellate in the circulating blood.

The Adrenalin Index of the Suprarenal Glands.—SYDENSTRICKER, DELATOUR, and WHIPPLE (*Jour. Exper. Med.*, 1914, xix, 536) have made a study of the adrenalin index, by which is meant the amount of adrenalin in milligrams per gram of the gland. Of the more accurate and sensitive methods for the determination of adrenalin Sydenstricker, Delatour, and Whipple have found the chemical colorimetric method the best. They have found that, as a rule, both adrenal glands in the same individual contain about the same amount of adrenalin per gram, the normal figures being 0.35 to 0.5 of a milligram, provided autopsy takes place shortly after death. In experimental work a low index was found, especially during the intoxication associated with intestinal obstruction. Animals, injected with a sublethal toxic dose of the poison found in closed duodenal loops, show after recovery a rise of the adrenal index to a point considerably above normal. The index falls to a low level as the result of liver poisons and is especially lowered after extirpation of the pancreas. It was found in pernicious anemia that the index is abnormally high, reaching in one case to twice the normal. This is of particular interest by reason of recent views put forward which indicate that the spleen and adrenal may be concerned in lipid metabolism which is thought to be profoundly disturbed in this disease. In diseases of the kidneys, heart or bloodvessels associated with high blood-pressure no constant variation in the adrenalin index was detected.

A Strain of Spirochetes Isolated from the Central Nervous System.—NICHOLS (*Jour. of Exper. Med.*, 1914, xix, 362) describes a strain of spirochetes recovered from the cerebrospinal fluid in a case showing central nervous system symptoms in the secondary stage of the disease. The patient had had some treatment with salvarsan. The strain was secured by the injection of 3 c.c. into dogs' testicles. Morphologically the organism was of the typical thick type described by Noguchi. Of the animals injected, half showed definite local symptoms, and disorders of the eyes were especially common, notably keratitis. Similar injections made with the spinal fluids from five cases of general paresis were without positive results, but sixteen inoculations with an emulsion of the cortex secured from cases of paresis gave weakly positive results in five instances. Nichols points out that the first strain obviously is different from the others for it never manifested any neurotrophic characters and even when inoculated into the brains of apes it failed to produce lesions.

The Relation of the Blood Sugar During Carbohydrate Cures.—J. MENKE (*Deutsch. Arch. f. klin. Med.*, 1914, cxiv, 209), using Bang's method, has studied the effect of carbohydrate cures on the blood sugar in diabetes. The work was carried out carefully and in considerable detail and is summarized as follows: (1) Determined hourly, the blood sugar of the diabetic shows great variations which, without regard to the severity of the case, are influenced on the one hand by the taking of food, on the other by the activity of the kidneys, since it was found that a fall of the blood sugar was co-incident with the excretion of sugar by the kidneys. (2) The absence of parallelism between the intensity of the glycosuria and the height of the blood

sugar concentration is confirmed. The results obtained make it probable that the kidneys are actively concerned in the excretion of the sugar. (3) The fasting value is often surprisingly high. In cases of diabetes of moderate severity or in severe cases, the differences are too small to serve as a basis for determining the severity of the disease. (4) From his numerous observations, the author concludes that noon is the most suitable time of day for determining the blood sugar. There is no essential difference between wheat and oatmeal, either as regards the height of the rise in blood sugar or the rapidity of the rise. (6) In determining the result of a carbohydrate cure or the finer indications for the same, estimations of blood sugar as yet have been of little value.

On the Effect of Dietetic Cures upon the Blood Sugar in Diabetics.—

L. WOLF and S. GUTMANN (*Ztschr. f. klin. Med.*, 1914, lxxix, 394), using Bertrand's method, have investigated the glucose content of the blood in its relation to diet in the treatment of diabetes in thirty-five cases. They have made simultaneous studies of the sugar and acetone bodies in the urine. Six of the thirty-five cases were complicated by chronic nephritis. In the twenty-nine non-nephritic patients, the use of a carbohydrate-free diet invariably led to a decline in the blood sugar. The percentage of decrease was in general proportional to the severity of the cases. Four of the mildest cases attained normal quantities of sugar in the blood. The moderately severe and severe cases reached a certain level of blood sugar concentration after a time; in a general way the degree of concentration corresponded to the severity of the disease and was maintained with a rather striking consistency. The severe cases ordinarily showed a more marked rise in the blood sugar following the administration of carbohydrate than the mild cases. In a few patients having complications (four with pulmonary tuberculosis, two with cirrhosis of the liver and three with arteriosclerosis) no deviation from the results for uncomplicated cases was found. When the blood sugar level characteristic of a given case had been obtained, restrictions of the supply of protein (through vegetable days or fat days) in the severe cases caused no decrease in the blood sugar even though a glycosuria had been caused to disappear. Oatmeal days, when they caused any change at all, produced a slight rise in the blood sugar. In four patients who died in coma, it was found that there was a rise in the blood sugar even though hunger days preceded the withdrawal of the specimen of blood for examination. The rise must be attributed to disturbances of the intermediary metabolism. In the six patients with nephritis complicating the diabetes, the quantity of blood sugar varied with the variety of renal disease. All of the nephritics retained a hyperglycemia, even though the glycosuria yielded promptly to dietetic treatment. In none of them could a constant level for blood sugar be obtained. In two with arteriosclerotic contracted kidneys, variations in the quantity of sugar occurred quite independently of carbohydrates in the food. Two patients with chronic interstitial nephritis exhibited an accumulation of blood sugar and of nitrogen, though the urine remained sugar free. Finally, two patients with marked parenchymatous nephritis showed a definite rise after a preliminary fall in the blood sugar.

SURGERY

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Favorable Influence of Röntgen-ray Stimulation in the Healing of Fractures.—FRAENKEL (*Zentralbl. f. Chir.*, 1914, xli, 1105) calls attention to previous communications on the favorable influence of the Röntgen rays on pleuritic thickening, on the dissolution of adhesions in peritoneal tuberculosis and on its influence in some gynecological and other conditions. He has tried it in eight cases of fracture. In a two-year-old child with a comminuted fracture of the second phalanx of the little finger and a six-year-old boy with a similar fracture of the first phalanx of the index finger, from careful exposure to the Röntgen rays, complete union was obtained in one case in eight days and in the other in ten days. In a third child with a transverse fracture of the radius and an oblique splintered fracture of the ulna, in six sittings with exposure of the fractures to the rays on all sides, the boy who was eight years old had a well-developed callus formation and consolidation of the fracture. The other cases which were in adults showed similar rapid healing. A one-and-a-half-year-old child had her thumb crushed under a heavy lid, a comminuted fracture of the first phalanx resulting. An attempt had been made to fix the fracture by sutures and silver clamps, and when the Röntgen-ray treatment was begun, gangrene threatened. After repeated exposures the threatened gangrene subsided, but the child later fell on the thumb, the therapeutic effect of the Röntgen rays was lost, and the thumb was amputated.

A Clinical and Experimental Contribution to Operation for Movable Kidney.—TICHY (*Deut. Zschr. f. Chir.*, 1914, cxxx, 17) made a study of this subject based upon an operation performed by König, as follows: The kidney was exposed by a lumbar incision. At the upper pole of the kidney in the fibrous capsule two frontal incisions about 1.5 cm. long were made, anteroposteriorly, about 4 cm. apart. Between the two the capsule was carefully undermined. Then from the external surface of the twelfth rib which had a well-developed periosteum, a strip of the latter was separated, about 1.5 cm. wide and 6 cm. long. It was divided anteriorly and the free end passed under the bridge of separated kidney capsule so that the surface of the periosteal strip separated from the rib lay in contact with the parenchyma of the kidney. The periosteum was then sutured on itself and to the rib so

that the kidney hung from it. The fibrous capsule was also split on the convexity of the kidney and its free edges sutured to the fascia. Gauze was lightly packed against the kidney and the wound closed to its lateral angle. A good fixation of the organ was thus obtained. Histological examination showed that the periosteum healed firmly to the capsule and kidney without any change in the structure of the kidney.

A Study of Malignant Tumors of the Testicle, Especially of the Epithelial Variety.—SÉKAGUCHI (*Archiv. gen. d. Chir.*, 1914, viii, 641) made a study of malignant tumors of the testicle based upon 32 tumors. The large-celled variety was the most frequent, 23 out of the 32 tumors being of this kind. The typical large-celled tumors of the testicle are epithelial and peculiar to the testicle. He believes that they are derived from the adult epithelium of the canals. The presence of cartilaginous tissue (existing in 2 cases) is explained easily by a metaplasia of the inflamed connective tissue with the appearance of hyaline tissue which presents all the forms of transition into cartilaginous tissue. Sarcoma of the testicle is rare (only one case among those of Sékaguchi). Simultaneous existence in the same testicle of carcinoma and tuberculosis was found in one case. There was no relationship between the two except that the tuberculosis may have developed secondarily to the carcinoma. The large-celled tumors developed usually between the thirtieth and fortieth years and between the fortieth and fiftieth years. The malignant epithelial tumors which resemble the adenoma in structure develop in infancy as well as in adult life. In 1 case this tumor developed in an old man. In 4 cases the tumor seemed to follow a traumatism. In 1 case it was related to an ectopic testicle.

The Treatment of Surgical Tuberculosis with Tuberculomucin (Wileminsky).—GOETZ and SPARMANN (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1914, xxviii, 53) discusses his results with the use of this new specific preparation in 54 cases of ambulatory tuberculosis. These included 17 cases of lymphoma, 12 of caries, 11 of fungus, 10 of multiple foci, 1 of tuberculous epididymitis, and 3 cases in which the differential diagnosis between tuberculosis and lues was doubtful. He regards the tuberculomucin as an efficient aid in surgical forms of tuberculosis. Of 44 cases, of which only one showed a lung involvement of mild grade, in 22 the results varied from improvement to cure. In all, the first puncture reaction was considerable. One case healed after the first reaction but recurred nine and one-half months later. Of the remaining 26 cases, 11 remained uninfluenced and of these 3 showed only a slight first reaction. The others grew worse and of these only 2 showed a slight first reaction. One died a long time after the beginning of the treatment. The first reaction has a prognostic importance. Mild or absent reaction from the initial dose of 3 to 6 mg. of the tuberculomucin appeared in such cases as were therapeutically uninfluenced or succumbed to the tuberculosis within the next four months. A considerable or strong first reaction is observed in cases in which are favorably influenced by the treatment, although it may be seen in cases unfavorably influenced. Of the various forms, those with localization of the

tuberculous process in bones have the best prospect of healing. Tuberculous lymph nodes with apparently the same clinical symptoms, differ so much in response to the treatment that it is difficult to estimate clearly the value of this specific therapy in connection with this form of surgical tuberculosis.

Gastric Ulcers Remote from the Pylorus.—FAULHABER and REDWAY (*Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1914, xxxviii, 150) discuss this subject on the basis of 52 cases operated on by Enderlens. Gastro-enterostomy was performed in 10 cases with one death; wedge-shaped resection in 3 cases without mortality; the Billroth II operation in 9 cases with one death; and circular resection in 30 cases with two deaths. In the histories of patients with gastric ulcers remote from the pylorus, the long duration and periodicity of the trouble is striking. Neither the history nor the clinical examination suffices for the localization of the ulcer, although the so-called "late pain," *i. e.*, a pain coming on three to five hours after eating, in a general way, speaks against a gastric ulcer remote from the pylorus. At times the Röntgen ray examination for a topographical diagnosis of a deep ulcer of the body of the stomach, is of much importance. Gastro-enterostomy does not guarantee a sure cure of the ulcer nor a protection against dangerous complications, as perforations, hemorrhages, or jejunal peptic ulcers. The danger of carcinomatous change is not important and according to the writers' experience is not frequent. The radical resection methods deserve the preference in the treatment of these ulcers. Excisions or wedge-shaped resections are to be considered only when the more radical operation is prevented and are most successful when combined with gastro-enterostomy. Resection of the middle of the stomach gives especially favorable results and provides good physiological relations. The chemical conditions in the stomach are to be considered in the choice of the operation to be done. When the percentage of acids is high a considerable portion of the stomach should be removed. The Billroth II resection probably deserves the preference in these cases.

Tarsalgia.—MERRILL (*Surg., Gynec., and Obst.*, 1914, xix, 67) says that depression in power and tone of muscles combined with abnormal poise of the body in weight-bearing, results in strain of muscles, or groups of muscles, under greatest stress, produces relaxation of such muscles, and may cause spasm of opposing muscles or group of muscles. Under this condition of spasm the stress exerted on the os calcis by virtue of the relationship of the posterior tibial tendon to it, this bone is tilted upward relatively, producing a subluxation at the calcaneo-cuboid and the astragaloseaphoid articulations, and the angle at the juncture of the tarsus and antitarsus is increased, producing a higher arch of the foot than normal. The pain resulting from this condition is due to the irritation in the muscle, it being manifested in the muscle and referred to the insertion of its tendons; it is also due to the strain produced in ligaments which enter into the composition of the mediotarsal joint. He concludes: that such a condition is of static origin, generally combined with a systemic disturbance; that the condition of static subluxation of the mediotarsal joint has for its principal factor a contraction and shortening of the posterior tibial muscle, and is

generally associated with a depression of power and tone of the anterior tibial; that a fairly constant type of symptoms can be found; that it usually exists without a frank inflammatory process; that the condition will yield to prolonged rest or palliative measures, or both; and that a certain derangement of relationship of structures in the foot and leg and perversion of function, will produce a definite type of pain in the tarsus, or tarsalgia.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Leukemia with Roentgen Rays and Benzol.—PULAWSKI (*Wien. klin. Woch.*, 1914, xxvii, 611) reports a case of severe lymphatic leukemia complicated with nephritis treated by a combination of benzol and roentgenotherapy. At the beginning of the treatment the hemoglobin was 30 per cent. and the white cell count was 425,600 with 90 per cent. of lymphocytes. After six exposures to the Roentgen rays during a period of nine days the white cells had dropped to 137,400 and the hemoglobin had risen to 36 per cent. During this time the lymph nodes and spleen diminished slightly in size. The patient was then given benzol in doses of 3 gm. a day during a period of sixteen days. At the end of this period the white cells have fallen to 8400. During the last nine days of the benzol treatment the patient had fever and the general condition became worse. Roentgenotherapy was resumed, four exposures being given over a period of nineteen days. The white cells continued to diminish in number so that two weeks after the discontinuance of the benzol treatment, the white cell count was 1100. However, the lymph nodes and spleen became perceptibly smaller. During the benzol period, Pulawski observed that the albumin and casts disappeared from the urine. This is noteworthy because the administration of benzol has apparently resulted in a number of instances, in distinct kidney irritation. Under combined iron and arsenic medication with a few exposures to the Roentgen rays, the white cells rose to 2600 with a fall in the percentage of lymphocytes from 90 to 40 per cent. and a rise in the neutrophils from 10 to 49 per cent. The general condition improved as well as the blood picture; the lymph nodes diminished to normal size and the spleen became one-fourth of its former size. The anemia which was severe following the benzol course had greatly improved, the hemoglobin rising from 23 per cent. to 50 per cent.

Salvarsan and Neosalvarsan in the Treatment of Nervous Disease Due to Syphilis.—CRAIG and COLLINS (*Jour. Amer. Med. Assoc.*, 1914, lxii, 1955) say that while salvarsan has proved our most rapid

and most efficient agent in treating syphilitic nervous disease, the use of mercury, preferably intramuscularly, in the interval between doses of salvarsan, has proved highly desirable. They recommend the salicylate in a purified petroleum oil suspension for intramuscular injection. It is probable that the intermittent treatment will prove advantageous. By this is meant a succession of periods of treatment and periods of rest, each covering a number of weeks. The spirochete is thus not rendered immune or less sensitive to the specific therapy as may occur when treatment is continuous. In observing the progress of therapy and the decadence of the syphilitic process, the Wassermann reaction and the cell count are the most enlightening guides. Improvement in symptoms nearly always follows improvement in these. The author's state in their conclusions, that the nervous system may be the site of attack within a few weeks after the initial lesion. The earlier antisymphilitic treatment is instituted in syphilitic nervous diseases, the greater the probability of complete recovery.

The Diagnosis and Treatment of Cerebrospinal Syphilis.—STEWART (*British Med. Jour.*, 1914, 2783, 949) reports excellent results in the treatment of cerebrospinal syphilis by intraspinal injections of either salvasanized serum or of small doses of neosalvarsan combined with the intravenous administration of neosalvarsan. In every one of 11 cases of tabes the clinical signs improved, lightning pains and gastric crises subsided, sphincter control was improved, ataxia was frequently diminished, and in one patient the knee-jerks, previously absent, reappeared. In every case, save one, the lymphocytosis of the cerebrospinal fluid was markedly reduced. In this case, the cells of the spinal fluid increased slightly in number, but the lightning pains disappeared and ataxia completely cleared up. In speaking of the intracranial methods for introducing remedies with the cerebrospinal fluid. Stewart says that we should select those methods which are least likely to cause damage to the brain. For this reason cortical applications possess certain advantages over intraventricular injections. Further, when comparing intraspinal with intracranial administration, we have to bear in mind that a long series of treatments is necessary in order to properly treat a given patient, and we must consider whether we are justified in submitting a patient to the risks of repeated cranial operations, unless these can be shown to yield results which are materially better than those obtained by intraspinal injection. Stewart says that improvement in the condition of the cerebrospinal fluid is a useful index of arrest of the disease, but it must be remembered that, in general paresis at least, the cell count in the fluid may go down without any corresponding improvement in the mental symptoms. This is readily understood when one bears in mind that, even if the disease process be arrested, those nerve-cells and nerve-fibers which have been already destroyed, remain destroyed and cannot be regenerated. It is therefore of importance to select only those cases of general paresis which are in the early or toxic stage of the disease, before the cortex has become profoundly degenerated. The earlier the disease is recognized, the better are the prospects of improvement. Advanced cases with profound cortical degeneration are totally unsuitable. The most thorough method of attacking general paresis would be to

administer remedies concurrently by all three routes—intravenously, intraspinally, and intracranially. It is too early to claim that we yet possess a cure for tabes or general paresis, but Stewart believes that in suitable cases, much can be done to arrest both diseases. Whether such periods of arrest are permanent, time alone will show.

The Salvarsan Treatment of Progressive Paralysis.—RUNGE (*Deutsch med. Woch.*, 1914, xl, 998) compares the results obtained in the treatment of 175 cases of progressive paralysis with the older methods, mercury and the iodids, with those obtained by the use of salvarsan in 91 cases. Periods of improvement, which he designates as remissions, occurred only in 3.9 per cent. of 380 cases in which no treatment had been taken; in 9.3 per cent. of 140 cases treated with iodid alone; in 11.4 per cent. of 35 cases treated only with mercury; in 14 per cent. of 44 cases treated with a total dosage of 1 gm. salvarsan, and in 60 per cent. of 47 cases treated with larger doses of salvarsan, ranging from 1.0 to 10.5 gm. The percentage of remissions increased with higher dosage, which is shown by the fact that 28 per cent. of 72 cases given less than 3 gm. of salvarsan improved while 74 per cent. improved of the 19 cases given over 3 gm. of salvarsan. Of all patients who were not treated by salvarsan only 2 per cent. remained stationary for long periods of time while 30 per cent. did so after salvarsan. The general health of the patients treated with salvarsan improved remarkably as a rule, even when the mental symptoms were not favorably influenced. Runge advises the administration of salvarsan by repeated courses up to a total dosage of 5 or 10 gm. His practise has been to give repeated small doses at five-day intervals, but lately he has been convinced that an eight-day interval is safer. Some of the cases treated with salvarsan showed no improvement but most of these received only very small doses. However, he has found that even large doses of salvarsan fail to induce a remission in some cases and the disease, furthermore, may even grow more severe. Four cases of this series seemed to be made distinctly worse. However, the dosage had been only 0.2 to 1.5 gm., and Runge thinks that a more favorable result might have been obtained if the treatment had been more thorough. The author believes that the results are better when the treatment is begun in the early stages of the disease but good results may be obtained in a large number of cases, even when the symptoms are of long duration.

The Treatment of Leukemia with Benzol.—LIBEROW (*Therap. Monatsheft*, 1914, xxviii, 339) reports a case of myeloid leukemia treated successfully with benzol. The daily dose averaged from 1.5 to 2.0 gm., and toward the latter part of the treatment only 1 gm. The author emphasizes the fact that the administration of benzol should always be controlled by repeated blood and urine examinations. No unfavorable effect was observed on the number of red blood cells and the hemoglobin. The red cells rose and kept above 5,000,000 and the hemoglobin remained at 62 per cent. When the white cells had dropped to 13,000, Liberow reduced the dose of benzol and there was no further fall in the number of leukocytes. The patient was a woman, aged thirty-four years, with marked ascites due, according to the author,

to probably pressure on the portal vein by a myeloid tumor. The ascites disappeared which he attributes to absorption of the leukemia and consequent relief from pressure.

A Method by Which Remedial Agents may be Mingled with the Spinal Fluid.—BALLANCE (*Lancet*, 1914, clxxxvi, 1525) describes the method in detail by which he introduced salvarsanized serum on five occasions into the lateral ventricle; twice in two patients and once in a third patient. No ill effects have occurred from the injection of the serum but Ballance says that only a large experience could justify a claim that this method would cure or arrest cerebral or spinal disease, as typified in general paresis or tabes.

The Intrathecal Injection of Salvarsanized Serum.—SPENCER (*Lancet*, 1914, clxxxvi, 1531) concludes that the intrathecal injection of salvarsanized serum offers a hopeful method of treating and arresting the progress of tabes and other parenchymatous diseases of the spinal cord. Before its introduction these cases resisted all efforts and finally drifted into the asylums and work-houses. A cure of the lightning pains can almost definitely be promised. The injections, if carried out with especial aseptic care and technique do not endanger the patient's life. There is a great future before this treatment when further work has been done in perfecting it. The cure of a condition, which has previously baffled all efforts, merely because the pathology has not been fully understood, is now possible by working on definite scientific lines.

The Intrameningeal Treatment of Tabes and Cerebrospinal Syphilis.—BOGGS and SNOWDEN (*Arch. Int. Med.*, 1914, xiii, 970) reports eight cases of cerebrospinal syphilis treated by intrameningeal injections of salvarsanized serum. The technique used by the authors differed in one important point from that recommended by Swift and Ellis. They injected undiluted serum in amounts of from 25 to 35 c.c. after preliminary intravenous injection of 0.6 gm. of salvarsan. Thus the average single dose was about double that given by Swift and Ellis. The authors state that, from the results in their series of cases, it is evident that the intraspinal method is a step forward in the treatment of tabes and cerebrospinal syphilis. The patients were uniformly relieved from pain, and as far as locomotion was concerned there was a slow but definite improvement, in some instances amounting almost to restitution to normal. In this respect their cases seemed to do better than those of Swift and Ellis, perhaps on account of the larger doses of serum. The psychic effect of the treatment was also marked. The patients became encouraged by the quick relief of pain and the first improvement in the control of motion and were faithful in their efforts to use the legs and practice walking, stair climbing, etc. The nutrition also rapidly improved under these stimuli. The effect of the treatment on the cerebrospinal fluid was very striking. The cell count first fell to normal, the Wassermann reaction becoming negative some time after the cells were reduced. The Noguchi reaction seemed of less value as an indication of improvement, since such large amounts of globulin were injected into the spinal canal. The authors

observed that the Noguchi reactions were positive, in most instances, after the cell count and Wassermann indicated a normal fluid. In the cases treated with the undiluted serum the reactions were sometimes more severe than those reported by Swift and Ellis—pain in the abdomen, legs and rectum, with occasional nausea and vomiting or dizziness, and in a few instances a little fever. They do not feel, however, that these constitute any contra-indication to the larger doses of whole serum, especially in the light of the apparently greater benefit to the patient.

PEDIATRICS

UNDER THE CHARGE OF

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Salvarsan and Neosalvarsan in Hereditary Syphilis.—J. L. BUNCH (*Brit. Jour. Child Dis.*, 1914, xi, 297) shows that the arsenical preparations have not displaced mercury in the treatment of all cases of congenital syphilis. But where treatment has been omitted until the case is almost hopeless, or where the symptoms are exceptionally acute or fail to respond to mercurial treatment, quite brilliant results can be obtained by the use of arseno-benzol or its derivative. The mortality of congenital syphilitics is very high. Of 1700 syphilitic pregnancies 1535 resulted either in abortion or death before the end of the first year. This shows that a more successful method of treatment than by mercury is necessary in a large number of these cases. Bunch gives the results of salvarsan treatment by a large number of investigators and they show an improvement over the mercury treatment alone. Neosalvarsan is more simple of preparation than salvarsan, but several important points are brought out in its application. The solution must be injected as soon as prepared. A sterile 0.4 per cent. saline solution made of freshly distilled water is best. The dose administered should be 0.15 gram. per kgrm. of body weight. The median, basilic or external jugular veins may be used for the intravenous method in young children. It is wise to start with small doses in all cases. Absolute immobilization of the patient is one of the great difficulties. It is unwise to inject neosalvarsan into patients with marked cerebral involvement or kidney disease. The drug is especially valuable in cases with skin lesions. In babies it is rarely necessary to use more than two or three injections, if more are necessary the intramuscular method should be used. The Wassermann reaction is of little use as a guide, usually remaining positive in spite of treatment while active symptoms are present. For rapidity of action and power of healing up syphilitic symptoms nothing superior has up to the present been discovered.

Auricular Flutter in Acute Rheumatic Carditis.—G. A. SUTHERLAND (*Brit. Jour. Child. Dis.*, 1914, xi, 337) describes an abnormal rhythm of the auricles in acute rheumatic carditis. Prognosis in this

condition is determined more or less by the degree of involvement of the myocardium. Another factor leading to cardiac failure is an abnormal rhythm of the heart. In acute carditis the ventricular rhythm is usually regular, as tested by the apex beat, pulse or tracing from the radial artery, whereas in the majority of cases abnormal rhythm is developed in the auricles and not in the ventricles. Sutherland mentions two cases in which an abnormal rhythm of the auricles was recognized only on taking a venous tracing in the neck. The auricular rate was greatly accelerated while the ventricle did not share in the acceleration. In other words, a number of auricular contractions failed to be followed by ventricular contractions. In both cases the auricular and ventricular rates were perfectly regular. The author explained the condition as probably due to ventricular inability to follow the auricle on account of the rapidity of the auricular beat, and not as due to heart block. If further investigation shows a disordered rhythm frequently present in acute carditis the treatment will be more hopeful, as a disordered rhythm of this nature responds more readily to digitalis than will a ventricle weakened by acute inflammation or toxemia.

OBSTETRICS

UNDER THE CHARGE OF

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Vicarious Menstruation Ceasing during Pregnancy.—HIRSCHBERG (*Zentralblatt f. Gyn.*, No. 26, 1914) reports the case of a Hungarian coming to live in Berlin, who menstruated not only in the usual manner but also through the breasts. When menstruation was established the vicarious discharge was at first watery in character. After the seventeenth year it became bloody, was attended by pain, began one or two days before the usual discharge and lasted one or two days longer. The discharge of blood was greater from the right than from the left breast. It could be increased by pressure, but escaped spontaneously. The patient had had two abortions, one at five and one at four months. During these pregnancies all menstruation ceased. After the last pregnancy the discharge from the breasts suddenly ceased without known cause and without disturbance.

The Danger of the Tampon in Placenta Previa.—REINHARDT (*Zentralblatt f. Gyn.*, No. 26, 1914) reported before the Gynecological Society of Dresden, 276 cases of placenta previa treated in the Dresden Clinic. He had observed the relative condition of those patients treated by the tampon and those without the tampon. Among those not treated by the tampon the morbidity during the puerperal period was 34 per cent., and the mortality from puerperal septic infection

0.7 per cent. Among those treated by the use of the tampon the morbidity was 53 per cent., the mortality from sepsis 4.3 per cent. From this and other experience he would abandon the use of the tampon even as a temporary measure to control hemorrhage until a patient could be brought into hospital. He would prefer to lessen bleeding by giving a full dose of morphia hypodermically. In discussion, Peters declared that the practising physician was not able to apply a tampon in a skilful and aseptic manner. He believed that the use of the bag in good hands, to temporarily control hemorrhage, was safer than a tampon. Richter had never seen the bag or tampon efficient in controlling hemorrhage. He believes that morphia first, and as soon as possible the emptying of the uterus, are the best means. Kehrer did not believe the aseptic use of the tampon possible outside of hospital.

Pernicious Nausea in Pregnancy.—BONDY (*Monatschrift f. Geb. u. Gyn.*, Band 39, Heft 6, 1914) describes the case of a married primipara, aged twenty-eight years, who suffered from pernicious nausea and vomiting in the early months of pregnancy. It seemed possible that some disease of the stomach was present and the patient was referred to the Medical Clinic in the Breslau Hospital, where the urine and blood were examined, the stomach irrigated, the patient fed by rectal injection and given oxalate of cerium and tincture of iodine by mouth. There was no improvement and the patient steadily lost weight. She was then returned to the obstetric clinic where 10 c.c. normal serum of pregnancy was injected into the muscles. Improvement immediately followed, and 15 c.c. of pregnancy serum was injected in the gluteal region. The patient's improvement was maintained, she was able to take solid food, recovered and was subsequently confined in the Clinic in normal labor with living child. Freunds has collected 8 cases of pernicious nausea treated by pregnancy serum, 6 of whom recovered. It is curious to observe that some of these recoveries followed the use of serum taken from the horse, and others the injection of Ringer's solution only. It seems difficult to believe that the introduction of the small quantity of alkaline substance in Ringer's solution could materially influence so serious a condition. Bondy also reports the case of a patient evidently toxemic with pernicious nausea, who died in spite of treatment including the interruption of pregnancy. The autopsy showed characteristic changes in liver and kidneys. As regards the frequency of genuine pernicious nausea, in the Breslau Clinic in 10,000 cases of labor, 21 of pernicious nausea have been observed. In the Munich Clinic Baisch found 20 cases in 20,000 pregnancies. In von Herff's Clinic, in 17,000 pregnancies, 30 cases of pernicious nausea. Contrary to usual opinion, the majority were married and multiparæ. The case of a multipara is reported who had once been treated for pernicious nausea by interrupting pregnancy. She returned and again pregnancy was interrupted by dilating with solid dilator, curetting with blunt curette and irrigation with alcohol. This was followed by collapse with slow recovery in coma. Two hours after profuse hemorrhage occurred partly controlled by the tampon. The patient slowly improved and left the Clinic against advice on the ninth day. On the day follow-

ing she was taken with unconsciousness and convulsions, brought to the medical Clinic with fever, albumin in the urine, casts and indican, with severe convulsions and spasm. Death speedily followed. Autopsy showed diphtheritic endometritis with thrombosis of both spermatie vessels, the heart muscle degenerated, the liver altered and hemorrhage into the substance of the kidneys. The writer draws attention to the many theories advanced to explain this condition, and inclines to consider it as toxic. In the matter of prognosis, each case must be studied individually, and the entire collection of symptoms critically reviewed.

The Biologic Test for Pregnancy.—PUPPEL (*Monatschrift. f. Geb. u. Gyn.*, Band 39, Heft 6, 1914) in 27 samples of blood from pregnant patients made 32 tests. In 16 the specimen came from a pregnant patient and of these 12 by first test gave a positive result. Several cases of pregnancy or abortion first gave a negative response, followed shortly by positive. In several cases some fault of the apparatus or inaccuracy in the technique was found. In 2 cases of the non-pregnant a positive result was followed later by a negative, and in 1 case of positive pregnancy a negative result persisted. In a case of abortion between the second and third month, where the uterus was cleared, a negative result was obtained two days after the treatment. A case of gonorrhea, 1 of two tuberculous pyosalpinx, 1 of amenorrhea after puerperal sepsis and one of beginning menopause gave negative results. He ascribes variations and failures to faults in technique rather than to an essential lack in the method.

Recovery After Shotgun Wound of the Abdomen and Pregnant Uterus.—DAVIS (*Amer. Med. Assoc.*, July 18, 1914), reports from the Massachusetts General Hospital of Boston, a case of an Italian woman, four months pregnant, admitted to Hospital about thirty minutes after receiving a shotgun wound of the abdomen at close range. On admission there was an irregular lacerated wound in the right lower abdominal quadrant. Two fists could be introduced into the abdominal cavity. Through this were protruding about four feet of small intestine. There was considerable oozing of blood. In the right groin about two inches below Poupart's ligament were two small punctured wounds. No powder burns nor wounds of exit could be found. There was no vaginal hemorrhage; the patient was shocked but the pulse and temperature were normal. Sterile towels wet with hot salt solution were immediately placed over the intestines. Morphine, $\frac{1}{4}$ gr. and camphorated oil 30 min. were given hypodermically, and one pint of normal salt solution injected under the right breast. At operation about 40 small perforations were found in the protruding bowel and in some places the shot could be palpated in the wall of the bowel. Through some of the perforations exuded gas and frothy fecal matter. The perforations were infolded with purse-string sutures of silk, several being included in one suture in many instances. At one point this caused constriction of the lumen of the bowel, but gas could be squeezed through. The intestines were carefully washed with warm salt solution and replaced. Considerable blood was found in the abdomen. The uterus showed a tear four inches long in the anterior wall, through

which protruded an umbilical cord leading to a four months' fetus, lying loose in the abdominal cavity. The placenta was removed manually from the uterus and the uterine wall closed with interrupted chromic catgut. The patient was given ergot hypodermically. No other abdominal injury was found. The abdomen was irrigated with warm salt solution and a cigarette drain placed in the right iliac fossa, and one in the pelvis. The abdomen was closed with loose approximation of the skin, and two additional cigarette drains in the subcutaneous tissue. The patient's condition at the end of operation was remarkably good and she was placed in the ward in Fowler's position, with rectal saline instillation. The patient made a steady and uninterrupted recovery. The skin edges of the wound sloughed and were repaired later under local anesthesia. A few shot were removed from the superficial tissues of the groin and abdominal wall. These corresponded to about No. 7 bird-shot. In about six weeks after the operation the patient was sent to the convalescent home, from which she went two weeks later in good condition. It is interesting to observe that the direction of the wound in the abdominal wall was transverse, while the rupture of the uterus was longitudinal, and there were no marks of shot wounds in the uterus. Apparently the rupture of the uterus resulted from sudden violent contraction at the moment when the patient was shot.

The Antitrypsin Test in Obstetric Cases.—HEINEMANN (*Monatsschrift f. Geb., u. Gyn.* Band 39, Heft 6, 1914) has applied antitrypsin solution test in 25 cases of pregnancy. In 15 a positive reaction was obtained, which was above the average, and in 10 a positive, an average reaction. A second 25 cases were studied, in which there was some doubt about the clinical signs of pregnancy; but 11 of these were available for later study. In 3 the antitrypsin test showed increased reaction, although there was no pregnancy. In 8 cases where the clinical signs pregnancy were present the antitrypsin test agreed. In 54 pronounced cases of carcinoma there were 4 negative results, and 3 of these were in cancer of the breast. In 7 cases where the test was positive clinical signs were not, and it was found that some other disease as tuberculosis, icterus, cirrhosis of the liver, or other constitutional disorder was present. In 12 cases of abnormal conditions of the pelvic organs, if fever was present the test was positive, in others negative, and in a case of myoma negative. Of the 50 pregnant women examined the clinical signs of pregnancy and the result of the test agreed in 47, and the conclusion is reached that the test is of decided practical value. A solution of trypsin 1 per cent. is used, and as an albuminoid controlled solution 2 per cent. of casein. The strength of the trypsin solution in effecting albuminoid is obtained by experiment, and this finally can be tested by an alcoholic solution of acetic acid which gives no precipitate, showing that the ferment has completely digested the albumin. Ferment and albuminoid are then tested in normal serum to observe the results. As a third step the serum of the patient who is studied is tested and compared with the serum of a patient positively known to be pregnant.

GYNECOLOGY

UNDER THE CHARGE OF

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Pelvic Varicocele.—In a paper read before the recent meeting of the American Medical Association, DARNALL (*Jour. Amer. Med. Assoc.*, 1914, vol. lxiii, p. 391) expresses the opinion that the existence of varicosities of the veins of the broad ligaments is a much more common condition than is generally recognized, and states in support of this that he has seen as many as ten cases in the past year. He thinks that in many instances women complaining of the following characteristic symptom-complex: aching pains in the pelvis and back, with dragging sensations, relieved by lying down, worse on standing or walking and at the menstrual periods, often with increased or too frequent menstruation; in other words, women suffering from all the symptoms of pelvic engorgement and irritation, but without any demonstrable lesion upon examination, are in reality victims of this condition of pelvic varicocele. The usual fate of these women is to be consigned to the large class of neurotics, whereas there is a real physical basis for their trouble. Darnall thinks the veins of the broad ligaments may become much enlarged during pregnancy, this being the most frequent origin of the condition. He recently had the opportunity during a Cesarean section of observing a worm-like tortuous bunch of veins in the right broad ligament, the main trunk being as big as the index finger; he believes that if after delivery involution of the uterus is not perfect there may be a failure on the part of these overdistended veins to regain their size and tone. This state of affairs is generally seen, therefore, in parous women, especially those with impaired perineal support, but it occasionally occurs in single women with retrodisplacements of the uterus. The history of these cases is usually that they have been to several physicians without relief, having in many instances finally had the abdomen opened for supposed intestinal kinks or membranes, even then the true cause being overlooked unless the veins of the broad ligament are carefully inspected. The diagnosis must of necessity be largely one of exclusion, based on the presence of the above mentioned symptoms, *without any gross pathologic lesion* that can be detected. The only satisfactory treatment is double ligation of the veins, with excision of the intervening portion. The author reports a number of cases in which this procedure was followed by complete relief of symptoms for varying periods up to one year after operation, this being the longest time for which any of the cases have been followed.

Cystoscopy in the Presence of Vesical Fistula.—The great difficulty of carrying out a satisfactory cystoscopic examination when there is a fistulous opening in the bladder wall is well known; unless the fistula be extremely small, the fluid used to distend the bladder immediately runs out, and no view can be obtained. Attempts to close the leak

temporarily by tightly tamponing the vagina are usually but indifferently successful at best, and fail completely when the fistula leads into the cervical canal. One author has suggested in such cases surrounding the cystoscope with a thin rubber condom, the cystoscope and condom being passed together into the empty bladder; the condom being then filled with fluid distends the bladder and spreads itself out on its internal surface, the examination taking place through this fairly transparent, thin sheet of rubber. It goes without saying that in many instances this maneuver is more ingenious than satisfactory. As KUBINYI (*Zeitschr. f. gyn., Urol.*, 1914, v, 1) points out, however, in certain cases of large fistula, situated in the upper portion of the bladder, a preliminary cystoscopic examination may be of the greatest importance in determining the exact location, shape and extent of the opening, and thus in laying out the plan of operation. In an extremely complicated case of this character he was able to obtain a perfectly satisfactory view of the interior of the bladder by means of the following procedure: The patient was a woman, aged forty years, who had passed through several difficult labors, and had acquired as a result both a rectovaginal and a vesicocervical fistula, the latter being of very considerable extent. After trying various of the methods mentioned above without success, Kubinyi placed a temporary purse-string suture about the vagina above the rectal fistula, using for this purpose novocain-adrenalin local anesthesia. By thus closing off the vagina, he formed of its upper part a closed pouch communicating through the cervical canal and fistula with the bladder, which he was then able without difficulty to fill with fluid, and thus to perform a perfectly satisfactory cystoscopic examination and determine exactly the conditions with which he had to deal. A few days later, under general anesthesia, he was able to close the fistula without great difficulty, and without any danger of injuring the ureters.

Treatment of Amenorrhea by the Intra-uterine Pessary.—A word in favor of this much discussed and (by many writers) much condemned method of treatment has recently been spoken by RIECK (*Zentralbl. f. Gyn.*, 1914, xxxviii, 1061), who reports his results in 22 cases of amenorrhea and oligorrhea, usually associated with some dysmenorrhea, but *not* due to chlorosis, severe anemia, or other constitutional disturbances. In all instances the condition came on at some time subsequent to puberty, and belonged in the class considered by Rieck as "idiopathic," *i. e.*, due to functional disturbances of the uterus, ovaries, or both. The patients varied in age from nineteen to forty years; in seven cases the condition was one of true amenorrhea, and in twelve of scanty menstruation (oligorrhea). In all these a complete cure was obtained by the use of the uterine stem, not only while the stem remained in place, but also after its removal for as long as it was possible to keep track of the patients. The remaining three cases were failures. In most cases the instrument was left in place for as long as from eight to twelve months, although the desired effect was usually produced much sooner. Two patients carried the stem six and eight years respectively, since they felt perfectly well, and did not return to the clinic for its removal. In one instance the instrument caused pain, and had to be removed after two weeks; in another

patient, a young girl with narrow vagina, the disk-like end of the stem caused some irritation of the vaginal wall, and the women who wore the pessary for eight years had an abortion; beyond these, no deleterious effects were observed. The author believes that most of the condemnation which in the past has been heaped upon the intra-uterine stem-pessary has been due to the faulty construction of the instruments used, as a result of which they were difficult to maintain in place, or caused injury to the vagina or uterus. The instrument which he uses is made of aluminum; it has a disk-like expansion which remains outside the portio vaginalis, a narrow portion which corresponds to the cervical canal, and a bulbous inner extremity, which lies in the body of the uterus and is tightly gripped by it. He lays great stress on the importance of this latter point, and says that in introducing the pessary dilatation should be carried only to the point that will just permit of pushing the bulbous end through the cervix, and that the instrument used must be of such size that the bulb will lie well above the internal os. He has found no advantage in having the stem perforated. When used properly, and the patients are kept under observation, the author believes the dangers following the use of this type of pessary to be negligible, and says that in an experience of many years he has never seen inflammatory trouble occur; he thinks that in the case where this has been reported, a sufficiently accurate diagnosis had not been made beforehand.

OTOLOGY

UNDER THE CHARGE OF

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Otospongiosis Otosclerosis.—Chronic progressive impairment of hearing is usually the result, according to LERMOYEZ (*Ann. des Mal. de l'Oreille*, xi, 5), of chronic non-suppurative processes originating in the tympanum or in the labyrinth, not infrequently the lesions are complex in their localized origin and the impairment of hearing may be characterized as tympanolabyrinthic in its causation. Earlier writers have noted the frequency of this form of lesion and determined its individual characteristics, and have attributed its evoked symptoms to a fixation or ankylosis of the stapes. Toynbee revolutionized otology by demonstrations of structural changes in the middle ear, which explained a large proportion of the so-called cases of nervous deafness as due to an impairment of mobility in the sound-transmitting apparatus through stapedal ankylosis, and von Troeltsch, confirming his observations, applied the term sclerosis to all the non-suppurative adhesive processes within the tympanum whatever their origin. It remained for Politzer, many years later, to demonstrate the real cause of many of the cases of gross impairment of hearing, slowly progressive, which had been included in the general mass of fixation changes of

tympanic origin, as due to a distinctive cause essentially characterized by changes in the bony capsule of the labyrinth, not an otitis but an osteitis definitely individualized but entailing, in most instances, as one of its secondary results, a fixation of the stapes and, in other instances, implication of the membranous labyrinth. These defined conditions continued to be confused, in otological nomenclature, under the title otosclerosis, until Ostman suggested for the pathological condition described by Politzer the name otospongiosis which has the definitive advantage of both clarity and precision since it portrays a progressive change which occurs in the osseous capsule of the labyrinth itself without implication of the petrous portion of the temporal bone, a condition due to the embryologic differentiation of the corresponding structures. The changes incident to this disorder in the bony labyrinthine capsule are divisible into three stages: (1) The interior of the Haversian canals becomes filled with an osteoid granulation tissue which substitutes itself for the original bony structure and supplants it. (2) This osteoid tissue disappears in its turn by lacunary absorption constituting temporarily in effect an intermediate bone. (3) Finally the medullary resorption cavities become filled with a third bony tissue, definitely new bone but passing through two evolutionary stages, at first compact and later becoming spongiform with resultant deformation of the labyrinthine capsule, the evolution constituting an osseous metaplasia and justifying the title given by Manasse, *otitis chronica metaplastica*. This transformation procedure has a predilection area, which is, however, by no means invariable. The preferential initiation region is that of the oval window, more especially anteriorly; its further propagation is either by continuity or by the appearance of isolated lesions affecting other portions of the capsule, but preferentially the region of the oval window without implicating the niche walls. There is a remarkable symmetry in the binaural exhibition of the locality of the lesions, not only those in which the region of the stapes is the main point of attack, but those in which the locations are multiple and aberrant. These observed facts are in accordance with the subjective symptoms as regards the hearing which varies in its manifestations according to the labyrinthine locality invaded, with the stapedal type predominant, and explains the symmetry of defect of hearing in the two ears in this class of cases. The predominance of the pathological changes in the region of the oval window results in the clinically long recognized ankylosis of the stapes, not a fibrous or adhesive fixation such as occurs sometimes in non-suppurative middle ear disease or as an after result of a suppurative process, but a bony fixation due sometimes to invasion of the spaces of the annular ligament by osseous tissue, to thickening and enlargement of the base plate which impairs mobility and to a fixation consequent upon osteophytic invasion of the oval niche, and while bony fixation of the stapes is not a constant accompaniment of otospongiosis, its frequency is such as to make the acoustic evidence of this condition clinically valuable toward the diagnosis of the intracapsular abnormality. Changes in the membranous labyrinth, especially the cochlea, are almost constantly observable as a consequence of the bony fixation of the stapes, but vary considerably in degree and in localization; they are, commonly, minute atrophic lesions in the cells of the spiral ganglion

of the modiolus and the terminal branches of the cochlear nerve in their distribution to the ganglion cells of the organ of Corti. Impairment of hearing due, at first, merely to an obstruction to the passage of the sound waves, by fixation of the stapes, becomes later, in the progress of the disease, complicated by impairment of function of the terminal nerve end apparatus itself with the production of a clinically, mixed type. The primary causes of otospongiosis are practically as yet unknown; one fact, however, is, according to Manasse, indisputable, namely, the absence of a local cause. Among general causes there are two theories which merit consideration; one that this peculiar lesion has its origin in specific disease either immediate or remote, and the other that it is directly referable to a lesion of the hypophysis productive of osseous distrophy analogous to the more exaggerated changes in acromegaly; the former theory has been long supported and combatted in the literature of the subject, the latter, proposed by Denker, is still under advisement and the subject of investigation; the influence of heredity and the observable effects of gestation and of exposure to inclemency and to cold evidence the measures of precaution which should be observed in these cases. On objective examination the drum head, and middle ear, as seen through the transparent membrane, present a normal appearance with exception of the roseate blush of the tympanic mucosa on the promontory and in the region of the oval window not always a constant symptom but, as noted by earlier observers, periodic in women with the access of menstruation and, in both sexes, incident to overfatigue or exposure to low temperature. Subjectively there is a decrease in duration of all tones aërially conveyed a prolongation in duration of hearing by bone conduction, a marked degree of depreciation in hearing for tones of low pitch and for the human voice, the hearing for tones of medium high pitch remaining contrastingly good, in the earlier stages. Later this hearing for high tones also decreases and the subjective circulation sounds become more pronounced. In the earlier stages of the labyrinthine change, with the increase in hearing by bone conduction, the voice of the patient, in speaking, while well modulated, is deficient in volume and only later becomes defective in its tone value as the nerve apparatus of the membranous cochlea becomes affected. Virtually otospongiosis is, as the author affirms, the *voli me tagere* of otology; it is a progressive and incurable disease, the evolution of which is usually enhanced by the local treatment regarded as applicable in cases of impairment of hearing incident to the chronic progressive nonsuppurative diseases of the middle ear. Its true nature is usually determined subjectively only after the labyrinthine disease has well advanced and when there remains for the patient only the application of hygienic arrestive measures and the acoustic reëducation. Local treatment by means of inflation of the middle ear, massage of the tympanum and operative interference in the nose and nasopharynx are all contra-indicated, the local stimulation and the adjacent local irritation incident to these measures serving only to stimulate the progress of the labyrinthine change. The general hygiene is prophylactic if it has for its basis as near an approach as possible to physiologic living, avoidance of extremes of temperature, especially of cold, moist air, open-air exercise in moderation, prolonged sleep and the avoidance of excitement and of

fatigue. Acoustic reëducation should be sought rather through the instrumentality of the human voice than by mechanical means, the understanding of speech visually should be encouraged as a compensatory measure, and the patient taught to live within the measure of the acoustic handicap.

The Clinical Pathology and Therapeutics of Subjective Noises in the Ear.—The importance of recognizing the existence of other than purely aural causes as factors in the production of this variable, and often burdensome symptom is emphasized by STEIN (*Monatschrift f. Ohrenheilkunde*, vol. xlviii, p. 5) in an extended and critical review of the literature of the subject coupled with the results of his own observations in a large number of cases, in which, in addition to a careful estimation of the aural condition, a thorough general examination was made with especial estimation of the influence exerted by changes in blood-pressure and by determinable abnormalities in the circulatory system. The general examination of patients suffering from severe subjective noises which have not yielded to the ordinarily remedial aural treatment shows, in a large proportion of the cases, subjective and objective abnormalities in the circulatory system and especially in the blood-vessels. The prominent disturbances of the circulatory system are either functional or organic, and among the latter arteriosclerosis plays the dominating role; the frequent occurrence of pathologic circulatory conditions in patients having subjective noises in the ears and the number of cases in which this symptom leads to the determination of such pathologic conditions, especially conditions resulting in increase in blood-pressure, emphasizes the importance of estimation of such conditions as factors in the cause of the subjective symptom. Disorders of the circulatory apparatus which may cause subjective noises are: (1) Vasodilatation in the arterioles, less frequently in the veins, within or in the neighborhood of the ear with an increased circulatory friction sound audible by auto-auscultation. (2) Imperfection in function of the heart and bloodvessels with consequent effect upon the activity and nutrition of the auditory nerve system. (3) Repeated or persistent narrowing of the arteries supplying the region inclusive of the auditory nerve and its distributions either as a result of vasoconstriction or of the narrowing of the vascular channels by sclerotic changes involving disturbance of nutrition and consequent degeneration. In the first class of cases the subjective noises would, under normal conditions, be comparatively unnoticed, but, with increased hearing by bone conduction, consequent upon impairment of sound transmission in the middle ear sound conducting apparatus, or with increased blood pressure, and correspondingly pulsatory increase in the region of the ear, the sounds become audible. In the second and third class of cases are to be found the subjective noises which are the product of an irritation in, or a degeneration of, the terminal auditory nerve apparatus. The classes of cases here enumerated are by no means to be regarded as individually delimitable but include often combinations of conditions and of symptoms; all illustrate the importance of the early recognition of general conditions of which the subjective aural symptom is an indication which it is important to regard as a possible precursory indication of a general condition and not a merely aural cause.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Pathological Rarities.—At the meeting of the German Pathological Association in Munich (*Centrabl. f. Allg. Path. u. path. Anat.*, Bd. 25, No. 10, May 31, 1914) VON HANSEMANN reported two cases of the formation of small shot-like masses in the appendix. Of the size of caviar, the masses were round, translucent, with a whitish core, and consisted of mucin and colloid. The appendix was enlarged, closed toward the cecum, perforated toward the peritoneum, and large numbers of these concretions were present. They are presumably found in widened mucous glands of the lining membrane, whence they are subsequently expelled. ROBERT MEYER showed a teratoma of the umbilical cord, which he describes as unique. Of the size of a child's head, it was situated in the course of the cord, 10 cm. from the cup of an umbilical hernia; it consisted for the most part of glia and endodermal parts, hair was absent, skin and sweat glands in small amount, as were bone and cartilage. Myxomas are found occasionally at the insertion of the cord, but this appears to be a very unusual tumor. Meyer considered it of somatic origin.

The Serum of Cold-blooded upon Warm-blooded Animals.—JURGELUNAS (*Zeit. f. Hyg. u. Infekt.*, 1914, Band lxxvi, Heft 3) details a number of operations upon the effects produced by the sera of cold-blooded animals upon warm-blooded. He found that serum from the eel, drake, pike, carp or frog are poisonous for mice, guinea-pigs, and rabbits, as evidenced by marked signs of malaise and fall in body temperature; the eel serum was more potent than the others above named. Such serums possess hemolytic powers over the blood corpuscles of man, and of the sheep as well as over the corpuscles of the rodents, but the poisoning properties are only indirectly connected with the hemolytic power, which is quickly and in great part lost by heating the serum.

Room Disinfection Against Tubercle Bacilli.—LAUBENHEIMER (*Zeits. f. Hyg. u. Infektionskr.*, Bd. 77, Hft. 1, 1914) has carried out a careful series of experiments with regard to the determination of proper means of disinfecting rooms infected with tuberculosis. Formaldehyde, sublimate 1 in 1000, and 5 per cent. cresol-soap, after nine hours application, are not sure disinfectants of dried sputum even in a thick layer, and of these formaldehyde is the best, if it be upon a hard surface that is not porous. Combinations of the above methods do not give any increased effectiveness; the soap or sublimate may even coat over the dried

sputum and thus protect it in some degree from the formalin. Formaldehyde and "phobrol"—apparently a new proprietary of the cresol group—give a more useful combination. Sublimate 1 in 200, and phobrol in 2 per cent. solution, if allowed five hours to work prove effective in killing the bacteria even in a thick layer.

The question is an important one; it is not known to the reviewer that any more effective method is used, in Canada at least, for the disinfection of rooms than the usual formalin method; and if it be quite ineffective for the killing of tubercle bacilli, the sooner the fact is generally known, the better for all persons concerned.

Hypertrophy of the Right Ventricle from Unusual Cause.—SCHÜTTE (*Centralbl. f. Allg. Path. u. path. Anat.*, Bd. 25, No. 11, June 15, 1914) describes a remarkable hypertrophy and dilatation of the right side of the heart occurring in a woman, aged seventy-four years, without general arteriosclerosis. The heart was large, death had occurred from cardiac insufficiency, but the enlargement was to a great extent right-sided. The cause of this was a remarkable inflammatory increase of the intima in the small branches of the pulmonary artery, especially those having a diameter of a quarter of a millimeter or less. There was an entire absence of emphysema or of disease of the valves of the left side of the heart, such as is usually found to cause arterial change of this nature. Several parallel cases have been recorded, usually under the title of idiopathic hypertrophy of the right ventricle.

The Intravascular Formation of Giant Cells.—WHITMAN (*Jour. Med. Res.*, January, 1914) has had opportunity of studying a giant-cell endothelioma of the gum and has been able to observe the intravascular formation of giant cells which has previously been observed in sporotrichosis. Whitman finds proliferation of endothelium of the bloodvessels, the nuclei proliferating from one side into the lumen surrounded by hyalin coagulum. The intima of the vessel may be recognized, still surrounding a lumen that is not yet completely obliterated, and blood cells may be seen in the process of phagocytosis of the new-formed cell. A subsequent thrombosis may destroy the outline of the vessels, and from this time the giant cell seems to lie in the tissue spaces. It owes the characteristic grouping of its nuclei to the fact that the proliferation of nuclei has occurred from one spot and has infiltrated a mass of preformed protoplasm. Whitman has also observed this mode of formation in blastomycosis and tuberculosis, although he does not consider that it is the only, or even the usual method.

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ORIGINAL ARTICLES

ULTIMATE RESULTS SECURED FROM SURGICAL INTERVENTION IN SIMPLE CASES OF CHOLELITHIASIS AND IN CHOLELITHIASIS DISCOVERED DURING OPERATIONS FOR OTHER CONDITIONS.

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THERE existed until within the last decade a widely prevalent view, borne out by the text-books of the time, that gall-stones could be present for prolonged periods without causing any manifest disturbance of the biliary or gastric function. This presumption was based upon a fallacious interpretation of the symptoms. That cholelithiasis, or even a marked cholecystitis, may exist without presenting the so-called classic symptoms is no longer questionable. Modern surgery has shed much light upon this subject and symptoms that were formerly regarded as essential for the establishment of a diagnosis of cholelithiasis are now looked upon as terminal rather than initial indications of biliary disorders.

At a meeting of the American Gynecological Society held in Boston a decade ago I reported several cases of cholelithiasis associated with gynecological lesions. From a summary of the views expressed at that time I quote the following:

"1. The usual statement that 95 per cent. of gall-stones produce no symptoms is fallacious, because it is based on autopsy and dissecting-room statistics.

"2. Bile possesses no bactericidal properties, for in the majority of cases of cholelithiasis microorganisms of a more or less pathogenic nature are discovered.

"3. Under these circumstances many vague symptoms, usually attributed to gastro-intestinal or general constitutional disturbance, may arise as the result of toxins elaborated about these foreign bodies in the gall-bladder.

"4. All clinicians admit that a wide hiatus exists in the clinical symptoms between the early formation of gall-stones and the so-called classic attacks of biliary colic with jaundice.

"5. Abdominal surgeons should carefully record all gastro-intestinal or hepatic symptoms, and any other vague epigastric pains, and these should be associated with the findings secured on examination of the gall-bladder, with a view to establishing a further link in the symptomatology of cholelithiasis.

"6. As cholelithotomy has been attended, in a large series of cases, with a mortality of less than 2 per cent., the removal of gall-stones during the performance of some other abdominal operation is not too hazardous an undertaking.

"7. This coincident operation should be undertaken only as the result of most careful surgical judgment, for if the patient is in a critical condition from a prolonged operation, or if the primary operation has been done for a septic condition, this additional operative procedure may be attended by serious consequences."

That the interpretation as expressed at that time has been sustained by later findings I believe the accompanying report of 159 gall-stone cases will amply prove. Since that time I have made an even more careful study of the symptomatology of cholelithiasis, and in only a small percentage of coincidental cases were these foreign bodies found to be innocuous.

In a paper recently published under the title of "Innocent Gall-stones a Myth," William Mayo says:

"Ten years ago we heard a great deal about 'innocent' gall-stones, which meant that gall-stones existed without symptoms, and that their presence was not suspected until postmortem examination brought them to light. We cannot now escape the conviction that the gall-stones did cause symptoms, and that we, as diagnosticians, and not the gall-stones, were 'innocent.'"

The late Dr. Richardson, in one of his last papers, entitled "The Diagnosis and Prognosis of Gall-stone Disease from the View-point of the Surgeon," takes up the symptomatology of cholelithiasis, and shows conclusively that in many cases there is no pathognomonic group of symptoms, but that the functional derangement incident to the presence of these foreign bodies may range from vague distress to the intense, cramp-like pain which the internist is so prone to call "gastralgia." This gastralgia in itself should be regarded as a "myth." The high-sounding term may satisfy the layman,

but certainly gastralgia is an infrequent symptom, exhibiting no tangible mechanical defects, and therefore it is most misleading and meaningless to both patient and physician.

Richardson expresses the view that these so-called innocent cases should be treated before they manifest the positive symptoms that indicate that an advanced stage of pathological change has taken place in the biliary system. In his expressive style he says: "Shall we wait for pathological changes of serious disease to become so characteristic that diagnosis is unmistakable? Shall the trend of medical and surgical thought be toward accuracy at the expense of safety? Shall the disease come to the surgeon or the surgeon go to the disease? Shall the lesion prevail until the surgeon, perforce, strikes a blow, or shall the surgeon assault, overwhelm, and destroy the lesion at its very inception? Shall we take that initiative so important and so favorable in matters of war, or shall we rest on the defensive?"

"The answer is simple it seems to me. With our utmost endeavor we must make our attack at the earliest possible moment, after we have, with reasonable accuracy located the enemy and ascertained his resources."

This, then, is the view-point of the surgeon. Now what of the physician? Their views are divided between a conservative medical and an active surgical intervention. In general, however, many excellent practitioners still exhibit a tendency to delay surgical intervention until the classic attacks set in. Too many are still dominated by the statistics of almshouses and hold to the now largely discredited belief as to the innocuousness of gall-stones.

In a Mütter Lecture on "Infection of the Biliary Tract," delivered in 1906 before the College of Physicians, the late A. O. J. Kelly, one of the most brilliant of the younger physicians of this country, very judiciously discussed this entire question, and unhesitatingly commended the wisdom of early intervention in these cases. I quote two paragraphs from this lecture, which will tend to show the general trend of his views concerning the dangers of cholelithiasis and the results of surgical treatment. He says: "Between the extreme of innocuousness or comparative innocuousness and quick and early disaster lie the great majority of cases of biliary infection." In discussing possible failure after surgical intervention he remarks: "The fact that the operative results are not always what were hoped for is not in itself a contra-indication to operation; on the contrary, these untoward results are often attributable rather to the fact that in many long-delayed cases the anatomical lesions are such as to be almost, if not quite, irremediable by any and all means at our command."

THE AFTER-HISTORY OF CASES. Surgeons during the last few years have modified many old and devised countless new operations and the immediate results of these procedures have

been widely studied. The ultimate results in cancer operations have been accurately traced, and in other diseases we have ascertained the percentage possibilities of cures; in many, however, no accurate statistics as to the remote results of surgical intervention have been secured. In conjunction with my assistant, Dr. Block, I have traced with great interest the results of a very large proportion of our cases of gall-stone operations, and have set down here in tabular form our findings. In one group are included cases in which an operation was performed for cholelithiasis without any associated gynecological condition. In the second group we have placed those cases in which gall-stones were discovered during a gynecological or other abdominal operation.

Of our series of 160 cases, in only 14 per cent. did we fail to secure accurate information as to the outcome. No case has been included in this list that was operated upon less than nine months previously.

Type of Operation. In our earlier practice it was our custom to suture the gall-bladder to the peritoneum of the anterior abdominal wall, thus shutting it off from the general peritoneal cavity. After considerable experience we discovered that in these cases biliary fistulas frequently healed slowly, and patients often complained of dragging or pulling pain at the site of the attachment for some time after their leaving the hospital. This method was, therefore, abandoned and now we use instead an improvised drainage-tube, which can be sutured securely into the gall-bladder. When this is done, the gall-bladder falls back into its normal position, and is not held in a constrained position against the abdominal wall. Since adopting this plan we have observed a marked improvement in the results, as shown by the prompt closure of the drainage tract and the subsequent comfort of the patient. By this means, too, perfect drainage has been secured and in those cases in which there has been persistent postoperative nausea the tube has served to facilitate the introduction, in a reverse way, of normal saline solution into the duodenum, as was recommended by McArthur. In all cases in which nausea persists after twenty-four hours we attach a saline reservoir to the drainage-tube, and under one foot of hydraulic pressure permit the fluid to drop slowly into the gall-bladder. Great care must be observed to avoid the slightest excess of pressure, which might induce a rupture about the point of insertion of the tube in the gall-bladder.

In our series of cases the drainage was usually maintained for ten days. This rule is, however, an arbitrary one, and in some cases the drainage period may be extended.

Within the last two years we have resorted to cholecystectomy in a greater proportion of cases, for experience has shown that if the wall of the gall-bladder is thick and indurated; or if it is dilated and very thin; or on inspection of the interior of the organ the

mucosa is found to be eroded or exhibits a strawberry mottling, cholecystectomy is the operation of choice. In those cases in which there are few or no symptoms, we have found that the removal of gall-stones with a ten days' drainage is followed by complete recovery and that there are no postoperative sequelæ. When, on the other hand, the gall-stones have caused more or less extensive pathological changes the outcome, so far as complete recovery is concerned, may be very unsatisfactory. Under such circumstances the patient continues to complain, and subsequent removal of the gall-bladder may be necessary.

From a study of the after-histories of these cases we are convinced of the necessity for resorting more frequently to cholecystectomy. Occasionally we have closed the gall-bladder after the removal of uncomplicated gall-stones, but we prefer to use a simple drain, thus obviating all danger of rupture of the gall-bladder and escape of bile into the peritoneal cavity.

From a review of this series of cases we conclude that:

1. Simple drainage is all that is necessary in cases of cholelithiasis in which there are no symptoms attributable to the presence of the stones.

2. When the gall-bladder is thickened or greatly dilated, or if it is the seat of the so-called "strawberry change," as described by Moynihan, cholecystectomy should be the operation of choice.

Through this analytical study of cases we have gained greatly in our knowledge of the best methods of dealing with the various lesions incident to gall-stones. Certainly mere drainage does not, as we formerly believed, cure every case of cholecystitis.

AS TO SO-CALLED REFLEX "GASTRALGIA," "INDIGESTION," AND "DYSPEPSIA." These terms are given prominence here in the hope that they will serve as a target for immediate demolition. In our series of cases many patients were referred to the gynecological wards for the repair of a lacerated cervix or perineum, or for the correction of a retroversion of the uterus, who exhibited clearly defined symptoms referable to the upper abdomen that were considered by the family physician as reflex manifestations, although an accurately traced history would have left no doubt as to their true significance. I am a pronounced pessimist as regards the belief that reflex symptoms in the upper abdomen emanate from gynecological lesions. In our teaching we constantly lay stress upon this point: "Locate your symptoms anatomically and then seek for the lesion in that locality." If this quest fails, then one may extend the diagnostic excursion to immediate or more remote organs.

In a very interesting case that came under our care recently the patient had suffered three years previously from characteristic attacks of gall-stone colic. A cervical laceration, which was considered to be the reflex source of these attacks, had been repaired

in a suburban hospital, the patient having been kept in bed for three weeks. The recovery was prompt and the cure apparently complete. All symptoms in the upper abdomen ceased—a triumph for this antiquated doctrine. A second baby was born and this was followed by a prompt return of the old symptoms. A small laceration had again occurred, and the patient's physician referred her to the gynecological department for relief of the condition by repair of the trivial laceration. Both physician and patient objected strenuously to even an exploration of the gall-bladder, and only when we refused to proceed with the operation without their permission was the request to explore acceded to. As a result, two hundred stones were found in the gall-bladder. Following the first operation the period of rest in bed had evidently brought about a quiescence of the gall-bladder symptoms, and only after the second pregnancy did they again become active. Many similar cases have occurred in our practice.

Latent gall-stones frequently become active subsequent to parturition. This is due, I believe, to the lessening of intra-abdominal pressure, with sagging of the gall-bladder and liver, thus causing a stagnation of bile, and precipitating an attack of cholecystitis. As a much larger percentage of gall-stones occur in child-bearing women than in those who have never been pregnant, and also because a larger percentage occur in women than in men, the gynecologist should be specially alert in studying the symptoms incident to disease of the organs of the upper abdomen. Serious error is especially likely to lurk within the shadow of a reflex doctrine, casting grave discredit upon the science of gynecology.

In gynecological cases manifesting coincident symptoms in the upper abdomen the gall-bladder, by far more frequently than any other organ, is the seat of disease. In a vastly larger series of gynecological cases gastric or duodenal ulcers or gastric carcinoma have been found so infrequently as to be regarded as almost negligible. Therefore when the upper abdominal symptoms are vague, and the possibility of diseases of the pylorus, duodenum, and gall-bladder is considered, the ratio of incidence is greatly in favor of the gall-bladder as the seat of the trouble. In our own cases the ratio is at least 100 to 1. In doubtful cases the diagnosis should invariably be cholelithiasis or cholecystitis, with the possibility of some one of these other lesions far in the background.

When should gall-stones be removed as an incidental part of a gynecological operation? We still adhere to the precautions laid down ten years ago, namely, that the coincident operation should be performed only as the result of careful surgical judgment, for, as stated previously, if the patient is in a critical condition from a prolonged operation, or if the primary operation has been a septic one, this additional surgical procedure may be attended by serious results.

Our series does not include a case in which stones were removed or even searched for if a septic focus existed in the pelvis. In every instance in which there is a record of a coincident operation for gall-stones having been performed in an inflammatory condition, this was done when the chronic stage had been reached and all activity had disappeared. A coincident operation is never performed in a purulent case even if there are decided symptoms of cholelithiasis.

In estimating the immediate and remote results of these combined operations, we have arranged our cases under three separate headings: First, simple gall-bladder cases, *i. e.*, those in which the surgical treatment was directed solely to the relief of the cholelithiasis; second, those cases in which some pelvic operation was performed and gall-stones were accidentally discovered; and third, gynecological cases in which there were unmistakable symptoms of associated gall-bladder disturbance.

So far as the immediate mortality is concerned, the first group, consisting of 55 cases, was attended by an immediate mortality of 4.3 per cent.; the second, by 7 per cent.; and in the third no fatality occurred.

As would naturally be expected, the possibility of wound infection is proportionately greater when two or more operations are performed; first, because of the greater number of surgical incisions, which, of course, increase the risk, and second, the greater hazard, in changing from one operation to another, of possible defects in technique. To overcome these dangers, separate sets of instruments and rubber gloves should be employed in each new operation. So far as the instruments are concerned, there is nothing fraught with so much danger as the repeated use of the surgical needle. In a simple hysterectomy, for example, a needle used in closing the uterine stump should be discarded, for there is always danger of it becoming contaminated from passage through the cervical canal; if this has occurred, it may, if used again, infect a fresh wound.

In these combined operations the greatest care should be observed in changing from one operative field to another. We never employ in the pelvic zone any of the instruments used in a plastic operation and the same precaution should be observed in the performance of a third operation in the upper abdomen.

Notwithstanding these precautions, our series of combined operations has shown a higher percentage of wound infections than the simple gall-bladder operations, in which the percentage of wound infections was 5.9; in the combined operations the rate was 9.7 per cent. in one series and 9 per cent. in the other. These figures cover any degree of wound infection from a small point to an extensive break in the wound. Another point to remember is that the greater the length of time consumed in these operations

the more likely to arise are untoward complications during convalescence. Thus postoperative vomiting and phlebitis are observed in larger degree in the combined operations. Pneumonia occurred only once in the entire series of cases.

In these days when hospital efficiency is arousing so much agitation, the number of days a patient spends in a hospital must be accounted for. In some hospitals the tendency has been to hasten convalescence, or, rather, to expedite the discharge of patients from the hospital. The test of efficiency should be the ultimate result secured, and not the brevity of sojourn in the hospital. I believe that a too early discharge of a debilitated or greatly enfeebled patient may lead to utter failure so far as the ultimate recovery is concerned. In free wards the personal equation must be most carefully estimated. In the case of a farmer's sturdy wife rapid convalescence may ensue after an early return home; in another instance if the patient lives in cramped quarters where the ventilation is poor and the food wretched, to hurry her home is to bring the final results in jeopardy.

In convalescence after surgical operations we have found the so-called neurasthenia to occur chiefly at the two extremes of the social scale—the pampered rich and the sorely impoverished. In the latter case the patient may never rise above the wretched environment unless she is well on the road to convalescence before she is discharged from the hospital. Further, we hold that no patient should be permitted to return to her home who possesses any disabling surgical complication. The psychic handicap to such a woman may frequently be quite insuperable. In cases of cholelithiasis we prefer, if possible, to keep our patients in the hospital until the fistula is closed, especially if they are not to be under our supervision after they leave the institution. In general, under the plan we now pursue, from eighteen to twenty-one days is the usual length of time these patients remain in the hospital.

The *causes of death* in our cases were as follows:

CASE I.—Cholangitis, which was produced by stones blocking the hepatic radicles in the liver substance, and pancreatitis, produced by a calculus that had ulcerated its way into the pancreas from the common duct. This stone was not discovered at the operation.

CASE II.—Extensive cystic destruction of the pancreas with chronic cholecystitis, death occurring from cholemia seventeen days later.

CASE III.—Umbilical hernia and chronic cholecystitis, death occurring from cholemia five days after operation. The output of bile steadily diminished, until it finally ceased entirely.

CASE IV.—Advanced pancreatitis with cholelithiasis, death from cholemia nineteen days after operation.

CASE V.—Cholecystitis, probable leakage about gall-bladder drain, death from a subphrenic abscess thirty-one days later.

CASE VI.—Chronic metritis with densely adherent tubes and ovaries, Lane's kink, concretion in appendix, and cholelithiasis. Hysterectomy, release of Lane's kink, appendectomy, and cholelithotomy were done. Death occurred from peritonitis five days later.

In summing up these cases we observe that four of the cases died from the destructive results of advanced cholelithiasis. In only two could death be attributed to any defect in the operative technique. In one there was a leakage with the formation of a subphrenic abscess; in the other a peritonitis. It is possible that these two deaths might have been avoided.

The point that the first four fatalities should drive home is that when pancreatitis of a chronic type supervenes the biliary condition sinks into insignificance beside the grave dangers that threaten from this sequel. In these cases the surgical mortality is extremely high. In none of the combined operations in which there were no symptoms attributable to gall-stones did a fatality occur.

ULTIMATE RESULTS. A. *Cases of Cholelithiasis Unassociated with Other Abdominal or Gynecological Lesions.* Of our series of fifty-five gall-stone operations not associated with other gynecological or abdominal conditions, 90 per cent. of results were traced. No case returned for a second operation, and none had been operated upon elsewhere.

Of this number 69.5 per cent. were cured, 15.2 per cent. were greatly improved, and 2.1 per cent. were not improved. Of the entire number, 8.6 per cent. died after leaving the hospital from extraneous conditions not connected with the surgical operation.

B. *Cases of Cholelithiasis with Symptoms Associated with Other Abdominal or Gynecological Lesions (seventy-seven cases).* Of this number, 78 per cent. were traced; 59.7 per cent. were cured, 17.5 per cent. were greatly improved, 1.7 per cent. were slightly improved, and 8.7 per cent. were unimproved. Since leaving the hospital, 3.5 per cent. died of intercurrent diseases not connected with the biliary operation.

C. *Cases of Cholelithiasis without Assignable Symptoms Associated with Other Abdominal or Gynecological Conditions (thirty-one cases).* Of this number 86 per cent. were traced, 64 per cent. were cured, 16 per cent. were greatly improved, 4 per cent. were slightly improved, and 8 per cent. (2 cases—both excessively neurotic) were worse than they had been before operation.

It is specially noteworthy that in the second class of cases, where there were unquestionable symptoms of diseases of the upper abdominal organs, in 13 there were visible changes in the appendices, ranging from mild to acute inflammations. Thus the error in diagnosis falls chiefly between appendicitis and cholecystitis. In

several of these cases the condition of the appendix gave rise to the acute symptoms which had precipitated the operation.

From this analysis we learn that the worst results occur among the combined cases in which there are manifest symptoms due to biliary changes. The ratio of the cures is in direct proportion to the severity of the symptoms. The weight of evidence most emphatically favors the early removal of gall-stones. The mortality will be very small, the proportion of cures very large, and the hazard of a return of the patient to the hospital for a second operation very slight. In the light of the results secured in this larger series of cases we believe that our stand of a decade ago, which favors the removal of gall-stones associated with other gynecological or abdominal lesions, whether they are producing symptoms or not, is amply sustained.

In the following summaries of case histories all patients have been accurately traced, and the final results, as tabulated, were obtained within two months of the preparation of this paper:

TABLE I.—Combined Operations with Gall-bladder Symptoms.
By FRANK B. BLOCK, M.D.

	No. of patients.	Days in hospital.	Convalescence.	Returned for second operation.	Cures.	Great improvement.	Slight improvement.	Unimproved.	Worse.	Death.
Displacement	25	29	Vomiting, 1 Phlebitis, 1 Infection, 2	2	10	2	1	2	0	4; 2 incident to operation.
Appendix . .	13	29	Vomiting, 1 Phlebitis, 1 Infection, 1	3	6	1	0	3	0	0
Fibroid . .	12	32	Infection, 3 Pneumonia, 1	1	9	3	0	0	0	0
Pelvic inflammation	9	27	0	3	2	0	0	0	1 (peritonitis).
Ovarian cyst .	7	28	1	3	0	0	0	0	0
Hernia (umbilical and ventrical)	4	26	Vomiting, 1 Infection, 1	0	2	0	0	0	0	2 (cholemia).
Stricture of rectum . .	1	29	0	0	1	0	0	0	0
Carcinoma of uterus . .	1	27	0	1	0	0	0	0	0
Floating kidney . .	1	28	0	0	1	0	0	0	0

TABLE II.—Combined Operations Without Gall-bladder Symptoms.

By FRANK B. BLOCK, M.D.

	No. of patients.	Days in hospital.	Convalescence.	Returned for second operation.	Cures.	Great improvement.	Slight improvement.	Unimproved.	Worse.	Death.
Fibroid	14	30	Vomiting, 2 Phlebitis, 1 Infection, 2	0	8	4	0	0	0	0
Displacement	5	25	0	1	0	0	0	2	0
Ovarian cyst	5	33	Cystitis, 1	0	3	0	0	0	0	1 (two years later; cause un- known).
Pelvic inflammation	3	25	Infection, 1	0	1	1	0	0	0	0
Displacement and hernia	2	24	0	2	0	0	0	0	0
Appendix	1	18	0	0	0	1	0	0	0
Cervical polyp	1	48	0	0	0	0	0	0	1 (cerebral hemorrhage six years later).

TABLE III.—Comparative Statement of Simple and Combined Gall-bladder Operations.

By FRANK B. BLOCK, M.D.

	Simple gall-bladder operations.	Combined operations with gall-bladder symptoms.	Combined operations with- out gall-bladder symptoms.	Total.
Number of cases	55	73	31	159
Percentage of cases traced	84.0 per cent.	78.0 per cent.	86.0 per cent.	86.0 per cent.
Average age of patients	42 years.	39 years.	44 years.	41.7 years.
Average number of days in hospital	29.4	28.6	29	29
Complications of convalescence:				
Infection	5.9 per cent.	9.0 per cent.	9.7 per cent.	8.2 per cent.
Prolonged vomit- ing0	4.0 per cent.	6.4 per cent.	3.1 per cent.
Phlebitis	2.0 per cent.	2.6 per cent.	3.2 per cent.	2.5 per cent.
Pneumonia0	1.3 per cent.	.0	.6 per cent.
Returned for second operation0	9.5 per cent.	.0	4.4 per cent.
Postoperative his- tory:				
Cured	69.5 per cent.	59.7 per cent.	64.0 per cent.	63.8 per cent.
Great improve- ment	15.2 per cent.	17.5 per cent.	16.0 per cent.	16.1 per cent.
Slight improve- ment0	1.7 per cent.	4.0 per cent.	1.5 per cent.
Unimproved	2.1 per cent.	8.7 per cent.	.0	4.6 per cent.
Worse0	.0	8.0 per cent.	1.5 per cent.
Died:				
In hospital	4.3 per cent.	7.0 per cent.	0	4.6 per cent.
Outside hospital, incident to oper- ation0	1.7 per cent.	0	.7 per cent.
Independent of operation subse- quent to dis- charge from hos- pital	8.6 per cent.	3.5 per cent.	8.0 per cent.	6.1 per cent.

TABLE IV.—SUMMARY OF CASE HISTORIES.
BY FRANK B. BLOCK, M.D.

SIMPLE GALL-BLADDER OPERATION.

Gyn. No. 95. April 19, 1900. Aged forty-seven years. *Symptoms*—indigestion, four years; flatulence; dragging pain after eating; colic; vomiting. *Clinical diagnosis*—cholelithiasis; intestinal adhesions. *Operation*—cholecystotomy; release of adhesions. *Convalescence*—normal; in hospital thirty-two days. *Postoperative history*—complete cure.

Gyn. No. 396. September 31, 1901. Aged thirty-three years. *Symptoms*—dysuria; backache; colic; jaundice; tenderness over gall-bladder; diarrhea. *Clinical diagnosis*—R. V. O.; cholelithiasis. *Pathological diagnosis*—chronic cholecystitis. *Operation*—cholecystomy. *Convalescence*—normal; in hospital thirty-two days; *Postoperative history*—cannot locate.

Gyn. No. 552. April 10, 1902. Age not given. *Symptoms*—not given. *Clinical diagnosis*—cholelithiasis; abdominal adhesions. *Pathological diagnosis*—gall-stones. *Operation*—cholecystostomy. *Convalescence*—stitch abscess; in hospital thirty-seven days. *Postoperative history*—complete cure.

Gyn. No. 887. April 17, 1903. Aged twenty-two years. *Symptoms*—colic, three years. *Clinical diagnosis*—cholelithiasis. *Operation*—cholelithotomy. *Convalescence*—stitch abscess; in hospital thirty-six days. *Postoperative history*—cured.

Gyn. No. 1083. November 23, 1903. Aged fifty-one years. *Symptoms*—colic and jaundice; two years; pain in hepatic region. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—cholelithiasis; cholangitis; chronic pancreatitis. See autopsy report. *Operation*—partial cholecystectomy. *Convalescence*—continual nausea, vomiting and prostration; death on thirtieth day. *Postoperative history*—autopsy; stones in pancreatic duct and hepatic radicles.

Gyn. No. 1118. December 29, 1903. Aged forty-nine years. *Symptoms*—indigestion, fifteen years; colic; clay stools. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholelithotomy. *Convalescence*—chill, $103\frac{2}{3}^{\circ}$; pain in back on fourth day; passed stones in stool eleventh day; in hospital twenty-eight days. *Postoperative history*—complete recovery.

Gyn. No. 1337. October 16, 1904. Aged thirty-six years. *Symptoms*—colic, chill and sweats three years; jaundice; clay stools. *Clinical diagnosis*—cholelithiasis; pyloric adhesions. *Pathological diagnosis*—gall-stones; catarrhal cholecystitis. *Operation*—cholecystectomy. *Convalescence*—bronchitis; pleurisy; lumbar abscess (intraperitoneal); in hospital sixty days. *Postoperative history*—patient cannot be traced.

Gyn. No. 1405½. December 2, 1904. Aged thirty-seven years. *Symptoms*—colic three years; discomfort over gall-bladder. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholelithotomy. *Convalescence*—normal; in hospital thirty-nine days. *Postoperative history*—complete cure.

Gyn. No. 1469. March 21, 1905. Aged fifty-two years. *Symptoms*—gastric distress four months; jaundice; epigastric pain; vomiting. *Clinical diagnosis*—empyema of gall-bladder; cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystotomy. *Convalescence*—incontinence of urine and hematuria following ethyl chloride anesthesia; in hospital fifty-six days. *Postoperative history*—complete cure.

Gyn. No. 1474. March 28, 1905. Aged twenty-six years. *Symptoms*—colic four years; vomiting. *Clinical diagnosis*—cholelithiasis; cholecystitis; intestinal adhesions. *Pathological diagnosis*—soft gall-stone material, no actual stones. *Operation*—cholecystotomy. *Convalescence*—influenza; in hospital thirty-three days. *Postoperative history*—complete cure.

Gyn. No. 1515. May 4, 1905. Aged thirty-two years. *Symptoms*—frequency of urination; backache; pains in both hypochondriac regions. *Clinical diagnosis*—cholelithiasis. *Operation*—cholecystostomy. *Convalescence*—several rises in temperature lasting a day or two at a time; in hospital forty-four days. *Postoperative history*—not located.

Gyn. No. 1576. August 10, 1905. Aged twenty-nine years. *Symptoms*—recurrence of symptoms nine months after operation; (see Case No. 950). *Clinical diagnosis*—intestinal adhesions; involving pylorus, transverse colon, and liver. *Operation*—release of adhesions to stomach and colon; excision of remains of gall-bladder. *Convalescence*—normal; in hospital twenty-six days; cured. *Postoperative history*—one year after operation had slight attacks of colic; now completely cured.

Gyn. No. 1651. November 14, 1905. Aged twenty-four years; *Symptoms*—pain in gall-bladder region and indigestion two years; constipation; vomiting. *Clinical diagnosis*—chronic cholecystitis; ptosis of liver. *Operation*—cholecystotomy. *Convalescence*—normal; in hospital thirty-seven days. *Postoperative history*—cured of gall-bladder symptoms; died three years later following intestinal obstruction from resection of colon, not due to previous operation.

Gyn. No. 1814. May 14, 1906. Aged forty-seven years. *Symptoms*—colic, thirteen weeks; jaundice. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—gall-stones; cholecystitis. *Operation*—cholecystotomy. *Convalescence*—normal; in hospital thirty-five days. *Postoperative history*—complete cure.

Gyn. No. 1844½. May 24, 1906. Aged sixty-five years. *Symptoms*—no symptoms preceding acute onset of gangrene. *Clinical diagnosis*—cholelithiasis; gangrenous gall-bladder. *Pathological*

diagnosis—acute cholecystitis; gall-stones. *Operation*—cholecystectomy. *Convalescence*—biliary fistula on discharge; in hospital thirty-five days; improved. *Postoperative history*—no recurrence of gall-bladder symptoms. Died of valvular heart disease four years after operation.

Gyn. No. 1983. November 10, 1906. Aged twenty-two years. *Symptoms*—pain in right hypochondrium three months; clay stools; vomiting; colic; jaundice. *Clinical diagnosis*—cholelithiasis; cholecystitis. *Pathological diagnosis*—chronic cholecystitis. *Operation*—cholecystotomy. *Convalescence*—normal; in hospital thirty-three days. *Postoperative history*—complete cure.

Gyn. No. 2107. March 19, 1907. Aged twelve years. *Symptoms*—attacks of colic for two years; vomiting; jaundice. *Clinical diagnosis*—cholecystitis; kinked gall-bladder. *Operation*—cholecystotomy. *Convalescence*—wound almost healed on discharge; in hospital twenty-one days. *Postoperative history*—complete cure.

Gyn. No. 2204½. May 26, 1907. Aged forty-four years. *Symptoms*—not given. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystotomy. *Convalescence*—normal; in hospital twenty-seven days. *Postoperative history*—complete cure.

Gyn. No. 2278. September 28, 1907. Aged fifty-two years. *Symptoms*—colic two months; tenderness and mass in gall-bladder area; loss in weight; has diabetes. *Clinical diagnosis*—cyst of pancreas (?); cholelithiasis. *Pathological diagnosis*—gall-stones; calcareous cyst. *Operation*—cholecystotomy; evacuation of cyst. *Convalescence*—continued nausea and vomiting; prostration; in hospital seventeen days; died of acetonemia.

Gyn. No. 2360. December 12, 1907. Aged thirty-two years. *Symptoms*—indigestion nine years; colic and jaundice lately. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—gall-stone. *Operation*—cholelithotomy. *Convalescence*—normal; in hospital fourteen days. *Postoperative history*—not located.

Gyn. No. 2483. March 31, 1908. Aged thirty-two years. *Symptoms*—jaundice; clay stools; indigestion; flatulence, one year. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystotomy. *Convalescence*—normal; in hospital twenty-eight days. *Postoperative history*—complete cure.

Gyn. No. 2529. April 29, 1908. Aged twenty-nine years. *Symptoms*—colic, four years; vomiting. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystotomy. *Convalescence*—normal; in hospital seventeen days. *Postoperative history*—complete cure.

Gyn. No. 2378. December 31, 1907. Aged twenty-eight years. *Symptoms*—colic, two months; flatulence; vomiting. *Clinical diagnosis*—cholelithiasis. *Operation*—cholecystotomy. *Convalescence*—normal; in hospital twenty days. *Postoperative history*—complete cure.

Gyn. No. 2396. January 10, 1908. Aged forty-two years. *Symptoms*—indigestion, thirteen years; sharp pain in left hypochondrium radiating to right shoulder. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholelithotomy. *Convalescence*—gall-stone discharged from wound on thirteenth day; in hospital twenty-eight days. *Postoperative history*—improved considerably; occasional attacks of pain.

Gyn. No. 2746. November 29, 1908. Aged forty years. *Symptoms*—colic, eight years; jaundice; vomiting; clay stools. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—gall-stones; cholecystitis. *Operation*—cholecystectomy. *Convalescence*—normal; sinus on discharge; in hospital fifty-six days. *Postoperative history*—much better than before operation; has occasional attack of "bilious cramps."

Gyn. No. 2853. February 17, 1909. Aged forty-five years. *Symptoms*—loss in weight and appetite; nausea; vomiting; brown vomitus; epigastric pain. *Clinical diagnosis*—carcinoma of stomach; cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystostomy; inoperable carcinoma of stomach. *Convalescence*—normal; in hospital twenty days. *Postoperative history*—died two years after operation from progressive cancer of stomach.

Gyn. No. 2898. April 15, 1909. Aged sixty-six years. *Symptoms*—colic, one and one-half years; vomiting; constipation. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—adenocarcinoma of gall-bladder, with gall-stones. *Operation*—partial cholecystectomy. *Convalescence*—normal; in hospital twenty-eight days. *Postoperative history*—not located.

Gyn. No. 2940. May 15, 1909. Aged forty-nine years. *Symptoms*—recurred six months after first operation (see Case No. 2394). *Clinical diagnosis*—Adhesions about gall-bladder; hemorrhoids. *Operation*—freeing of adhesions about gall-bladder; excision of one-half inch of fundus. *Convalescence*—tedious; occasional rise in temperature; in hospital thirty-five days; *Postoperative history*—indigestion; pain in gall-bladder area; severe headaches for sometime after operation now perfectly well.

Gyn. No. 2972. June 8, 1909. Aged thirty-seven years. *Symptoms*—colic, one year; jaundice; dark urine; flatulence; gastric irritability. *Clinical diagnosis*—cholecystitis; cholelithiasis. *Pathological diagnosis*—chronic cholecystitis. *Operation*—cholecystectomy. *Convalescence*—normal; in hospital twenty-seven days. *Postoperative history*—not located.

Gyn. No. 2998. June 22, 1909. Aged sixty years. *Symptoms*—pain in right hypochondrium, five weeks; mass over gall-bladder; jaundice; clay stools; painful urination. *Clinical diagnosis*—empyema gall-bladder; carcinoma common duct; gall-bladder and liver. *Pathological diagnosis*—carcinomatous metastasis to

lymphatic gland; gall-stones. *Operation*—partial cholecystectomy; inoperable carcinoma of gall-bladder and liver. *Convalescence*—severe pain in back; in hospital twenty-two days; unimproved. *Postoperative history*—continued to decline rapidly and died nine weeks after operation.

Gyn. No. 3007. July 3, 1909. Aged forty-five years. *Symptoms*—colic, one year; epigastric pain and tenderness; nausea. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—chronic cholecystitis; gall-stones. *Operation*—cholecystectomy. *Convalescence*—phlebitis left femoral vein; in hospital twenty-four days. *Post-operative history*—great improvement; occasionally recurrence of pain.

Gyn. No. 3011. July 6, 1909. Aged fifty-five years. *Symptoms*—general abdominal discomfort. *Clinical diagnosis*—intestinal adhesions; ventral hernia; cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystostomy. *Convalescence*—stitch abscess; in hospital thirty-nine days. *Postoperative history*—slow convalescence; complete cure.

Gyn. No. 3061. September 28, 1909. Aged sixty-five years. *Symptoms*—sciatica, three years; dizziness; nausea; swelling in right hypochondrium; clay-colored stools. *Clinical diagnosis*—cholelithiasis; hydrops of gall-bladder. *Pathological diagnosis*—chronic cholecystitis; gall-stones. *Operation*—cholecystectomy. *Convalescence*—normal; in hospital thirty-six days. *Postoperative history*—complete cure.

Gyn. No. 3266. April 4, 1910. Aged fifty-four years. *Symptoms*—colic, ten months; occasional vomiting. *Clinical diagnosis*—cholelithiasis; chronic cholecystitis. *Pathological diagnosis*—chronic cholecystitis; gall-stones. *Operation*—cholecystectomy. *Convalescence*—normal; in hospital twenty-two days. *Postoperative history*—complete cure.

Gyn. No. 3497. October 26, 1910. Aged forty-three years. *Symptoms*—colic, thirty years; vomiting; flatulence; jaundice; dark urine. *Clinical diagnosis*—gangrenous cholecystitis; cholelithiasis. *Pathological diagnosis*—chronic cholecystitis; gall-stones. *Operation*—cholecystectomy. *Convalescence*—slight septic temperature during convalescence; in hospital thirty-one days. *Post-operative history*—complete cure.

Gyn. No. 3635. February 16, 1911. Aged forty-six years. *Symptoms*—jaundice; vomiting; clay stools, six months. *Clinical diagnosis*—cholecystitis. *Operation*—cholecystostomy. *Convalescence*—slight septic temperature; in hospital twenty-one days. *Postoperative history*—complete cure.

Gyn. No. 3756. May 25, 1911. Aged fifty-two years. *Symptoms*—indigestion, four years; pain over gall-bladder; flatulence; colic; jaundice; vomiting; clay stools. *Clinical diagnosis*—cholecystitis. *Pathological diagnosis*—chronic cholecystitis; gall-stones.

Operation—cholecystectomy. *Convalescence*—normal; in hospital twenty-three days. *Postoperative history*—complete cure.

Gyn. No. 3758. May 26, 1911. Aged twenty-four years. *Symptoms*—colic; mucous fistula since operation (see Case No. 3666). *Clinical diagnosis*—chronic cholecystitis. *Operation*—cholecystectomy. *Convalescence*—normal; in hospital seventeen days. *Postoperative history*—complete cure.

Gyn. No. 3847½. August 20, 1911. Aged thirty-eight years. *Symptoms*—colic, nine years; gastric irritability; jaundice; vomiting; chill. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—chronic cholecystitis; gall-stones. *Operation*—cholecystectomy; *Convalescence*—marked postoperative shock; in hospital twenty-two days. *Postoperative history*—complete cure.

Gyn. No. 3961. November 13, 1911. Aged forty-six years. *Symptoms*—pain in gall-bladder region (see Case No. 2864½). *Clinical diagnosis*—chronic pericholecystitis. *Pathological diagnosis*—chronic cholecystitis. *Operation*—cholecystectomy. *Convalescence*—normal; in hospital nineteen days. *Postoperative history* (see Case No. 2864½). Pain in gall-bladder incision and gastric area; considerable hyperacidity.

Gyn. No. 3991. December 4, 1911. Aged twenty-nine years. *Symptoms*—colicky pain in gall-bladder region (see Case No. 3445). *Clinical diagnosis*—chronic cholecystitis; pericholecystitis. *Pathological diagnosis*—chronic cholecystitis. *Operation*—Cholecystectomy. *Convalescence*—stitch discharged through sinus; in hospital thirty days. *Postoperative history*—complete cure.

Gyn. No. 4143. March 27, 1912. Aged sixty-six years. *Symptoms*—indigestion forty-eight years; colic; jaundice; loss in weight. *Clinical diagnosis*—cholelithiasis; chronic cholecystitis; chronic pancreatitis. *Pathological diagnosis*—chronic cholecystitis. *Operation*—cholecystectomy. *Convalescence*—dizzy spells (myocardial); in hospital twenty-three days. *Postoperative history*—complete cure.

Gyn. No. 4146. April 1, 1912. Aged forty years. *Symptoms*—soreness in abdomen; increases by urination; duration seven years. *Clinical diagnosis*—cholelithiasis; kink of right ureter. *Operation*—cholecystectomy; exploratory incision over right kidney. *Convalescence*—febrile (slight); in hospital thirty-three days. *Postoperative history*—improved; no colic; complains of pain and fullness in incision, probably hernia.

Gyn. No. 4223. May 20, 1912. Aged thirty-six years. *Symptoms*—colic, six years; vomiting; jaundice; chills; fever. *Clinical diagnosis*—tuberculous cholecystitis; pericholecystitis; tuberculosis of liver. *Pathological diagnosis*—tuberculous cholecystitis; tuberculous perihepatitis. *Operation*—cholecystectomy; choledochotomy. *Convalescence*—superficial sinus on discharge; in hospital twenty-five days. *Postoperative history*—not traced.

Gyn. No. 4283. August 6, 1912. Aged twenty-seven years. *Symptoms*—typhoid; cholecystitis with empyema; typhoid, one month ago; colic since then with vomiting; constipation. *Clinical diagnosis*—cholelithiasis; empyema of gall-bladder; chronic cholecystitis. *Pathological diagnosis*—chronic cholecystitis; gall-stones; normal appendix. *Operation*—cholecystectomy. *Convalescence*—normal except slight sinus on discharge; in hospital twenty-four days. *Postoperative history*—complete recovery; complains of slight pain over incision.

Gyn. No. 4355. September 19, 1912. Aged fifty-six years. *Symptoms*—pain over gall-bladder, sixteen years; colic; vomiting; jaundice. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—chronic cholecystitis; gall-stones. *Operation*—cholecystectomy. *Convalescence*—normal; in hospital twenty-six days. *Postoperative history*—great improvement; no colic; soreness under shoulder-blade; somnolence.

Gyn. No. 4422. October 31, 1912. Aged thirty-eight years. *Symptoms*—colic, five years; vomiting; flatulence. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystectomy. *Convalescence*—small sinus on discharge; in hospital twenty days. *Postoperative history*—recurrence of colic two to three weeks after operation followed by complete recovery.

Gyn. No. 4550. January 21, 1913. Aged forty-eight years. *Symptoms*—epigastric fulness for two years; flatulence; loss in weight. *Clinical diagnosis*—cholelithiasis; pericholecystitis. *Pathological diagnosis*—chronic cholecystitis; gall-stones. *Operation*—cholecystectomy. *Convalescence*—normal; in hospital seventeen days. *Postoperative history*—not traced.

Gyn. No. 4565. January 29, 1913. Aged forty-six years. *Symptoms*—colic, two years; vomiting; dark urine. *Clinical diagnosis*—cholelithiasis; chronic pancreatitis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystostomy. *Convalescence*—normal; in hospital twenty-eight days. *Postoperative history*—complete cure.

Gyn. No. 4593. February 19, 1913. Aged forty-one years. *Symptoms*—indigestion and colic, two years; slight nausea; vomiting and jaundice. *Clinical diagnosis*—cholelithiasis. *Operation*—cholecystostomy. *Convalescence*—normal; in hospital twenty-four days. *Postoperative history*—complete cure.

Gyn. No. 4608½. February 28, 1913. *Symptoms*—not given. *Clinical diagnosis*—cholecystitis. *Pathological diagnosis*—chronic cholecystitis; gall-stones. *Operation*—cholecystostomy; choledochotomy. *Convalescence*—normal; in hospital twenty-four days. *Postoperative history*—complete cure.

Gyn. No. 4800. July 8, 1913. Aged thirty-eight years. *Symptoms*—colic, one and one-half years; vomiting; jaundice; constipation; indigestion. *Clinical diagnosis*—cholelithiasis. *Pathological*

diagnosis—gall-stones. *Operation*—cholecystostomy. *Convalescence*—normal; in hospital twenty-two days. *Postoperative history*—marked improvement; no colic; has constipation and pain in back.

Gyn. No. 4806. July 11, 1913. Aged forty-three years. *Symptoms*—indigestion ten years; dull pain in epigastrium; flatulence; constipation; loss of support from below. *Clinical diagnosis*—cholelithiasis; pericholecystitis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystostomy. *Convalescence*—normal; in hospital twenty-seven days. *Postoperative history*—cured of gall-stone symptoms. Condition did not permit plastic operation; will return for this later.

Gyn. No. 4828. August 21, 1913. *Symptoms*—indigestion and gall-bladder pain. *Clinical diagnosis*—cholecystitis. *Pathological diagnosis*—chronic cholecystitis. *Operation*—cholecystotomy. *Convalescence*—normal; in hospital fourteen days. *Postoperative history*—complete cure; gained twenty pounds.

Gyn. No. 4832. August 27, 1913. Aged forty-nine years. *Symptoms*—colic, twenty years; vomiting. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—chronic cholecystitis. *Operation*—cholecystostomy. *Convalescence*—attack of indigestion twenty-second day; in hospital twenty-six days. *Postoperative history*—considerable improvement, although she has recurring symptoms of a lighter degree.

COMBINED OPERATIONS WITH GALL-BLADDER SYMPTOMS.

Gyn. No. 368. September 2, 1901. Aged forty-five years. *Symptoms*—biliary colic, sixteen years; prolapsus uteri. *Clinical diagnosis*—R. V. O.; cholelithiasis; retroflexion; prolapsus. *Pathological diagnosis*—endometritis cervicis. *Operation*—cholecystotomy; plastic, suspension. *Convalescence*—distention and vomiting three days; in hospital thirty days. *Postoperative history*—complete cure.

Gyn. No. 583. May 12, 1902. Aged twenty-seven years. *Symptoms*—backache; pain in lower abdomen. *Clinical diagnosis*—cholelithiasis; intestinal adhesions. *Pathological diagnosis*—gall-stones; periappendicitis. *Operation*—cholecystostomy; release of adhesions; appendectomy. *Convalescence*—constipation; in hospital seventy-one days; improved. *Postoperative history*—unimproved; intense neurasthenia.

Gyn. No. 600. May 21, 1902. Aged forty years. *Symptoms*—colic, three attacks in past year; jaundiced; abdominal tumor. *Clinical diagnosis*—right ovarian cyst; cholelithiasis. *Pathological diagnosis*—gall-stones; cystadenoma ovarii pseudomucinosum glandulare. *Operation*—cholecystostomy; right salpingo-oöphorectomy. *Convalescence*—normal; in hospital twenty-five days. *Postoperative history*—not traced.

Gyn. 898. April 26, 1903. Aged thirty-six years. *Symptoms*—pain after urination; dragging pain; indigestion; colic; jaundice; clay stools. *Clinical diagnosis*—cholelithiasis; tubo-ovarian abscess. *Pathological diagnosis*—acute suppurative salpingitis; gall-stones. *Operation*—left salpingo-oöphorectomy. *Convalescence*—chill, 103½° F. Jaundice on fourth day; gone on seventh day; in hospital thirty-six days. *Postoperative history*—not traced.

Gyn. No. 950. June 20, 1903. Aged twenty-eight years. *Symptoms*—colic four years; tenderness over gall-bladder. *Clinical diagnosis*—cholelithiasis; parovarian cyst; erosion of cervix. *Pathological diagnosis*—endometritis cervicis. *Operation*—partial cholecystectomy; plastic; cystectomy. *Convalescence*—normal; in hospital twenty-five days. *Postoperative history*—returned for second operation (see Case No. 1576).

Gyn. No. 1069. November 1, 1903. Aged thirty-eight years. *Symptoms*—epigastric pain; indigestion. *Clinical diagnosis*—retroversion; cholelithiasis; cystic gall-bladder; R. V. O.; diastasis recti. *Pathological diagnosis*—gall-stones. *Operation*—cholecystectomy; suspension. *Convalescence*—adherent cicatrix; in hospital thirty-five days. *Postoperative history*—died of intestinal obstruction several months later.

Gyn. No. 1074. November 4, 1903. Aged forty-three years. *Symptoms*—pain over gall-bladder for three years; abdominal cramps before menstruation; one attack of colic. *Clinical diagnosis*—uterine fibroid; cholecystitis; empyema of gall-bladder; cholelithiasis; chronic appendicitis. *Pathological diagnosis*—fibromyoma uteri; chronic appendicitis; purulent cholecystitis; gall-stones. *Operation*—hysterectomy; appendectomy; cholecystectomy. *Convalescence*—normal; in hospital thirty-two days. *Postoperative history*—complete cure.

Gyn. No. 1105. December 11, 1903. Aged thirty years. *Symptoms*—indigestion; pain in epigastrium and vomiting for five years; attacks of pain right iliac fossa. *Clinical diagnosis*—right ovarian cyst; cholelithiasis. *Pathological diagnosis*—gall-stones; corpus luteum cyst. *Operation*—cholelithotomy; right oöphorectomy. *Convalescence*—normal; in hospital thirty-one days. *Postoperative history*—slow convalescence; incapacitated for one year; now perfectly well.

Gyn. No. 1152. February 7, 1904. Age not given. *Symptoms*—dysmenorrhea; abdominal pain for two years. *Clinical diagnosis*—appendicitis; metritis; cholelithiasis. *Pathological diagnosis*—hyperplasia of uterus; interstitial endometritis; obliterative appendicitis. *Operation*—hysterectomy; appendectomy; cholelithotomy. *Convalescence*—wound infection; in hospital thirty-three days. *Postoperative history*—not traced.

Gyn. No. 1197. March 24, 1904. Aged twenty-eight years. *Symptoms*—indigestion for twelve years; colic; vomiting; flatulence.

Clinical diagnosis—cholelithiasis; chronic appendicitis. *Pathological diagnosis*—chronic appendicitis. *Operation*—cholelithotomy; appendectomy. *Convalescence*—several stones washed out on eighth day; prolonged postoperative vomiting; in hospital thirty-six days. *Postoperative history*—great improvement; has nervous indigestion; considers operative result very successful.

Gyn. No. 1335. October 11, 1904. Aged forty-four years. *Symptoms*—colic with nausea and vomiting, eight years; clay stools; jaundice. *Clinical diagnosis*—cholecystitis; R. V. O.; lacerated cervix. *Operation*—plastic; cholecystotomy. *Convalescence*—normal; in hospital forty-five days. *Postoperative history*—well for eight years; then cholecystenterostomy was performed for intense jaundice from occlusion of common duct; died May 13, 1913; cancer (?).

Gyn. No. 1516. May 4, 1905. Aged fifty-six years. *Symptoms*—metrorrhagia, one year; frequency of urination. *Clinical diagnosis*—cholelithiasis; cervical polyp; lipoma of vulva. *Pathological diagnosis*—gall-stones; lipoma of vulva. *Operation*—cholecystectomy; removal of cervical polyp. *Convalescence*—biliary fistula on discharge; in hospital forty-eight days; improved. *Postoperative history*—complete cure; died six years later from cerebral hemorrhage.

Gyn. No. 1899. August 24, 1906. Aged thirty-one years. *Symptoms*—colic, seven years; constant dull pain; vomiting. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—chronic appendicitis; gall-stones. *Operation*—cholelithotomy; appendectomy. *Convalescence*—"sticking pain" in incision; in hospital twenty-eight days. *Postoperative history*—unimproved; reoperated upon elsewhere for adhesions.

Gyn. No. 1934. September 25, 1906. Aged thirty-six years. *Symptoms*—indigestion; frequent attacks of pain in gall-bladder region; has lost control of rectum. *Clinical diagnosis*—cholelithiasis; stricture of rectum by adhesions. *Pathological diagnosis*—chronic cholecystitis; gall-stones. *Operation*—cholecystectomy; cutting band in rectum. *Convalescence*—normal; in hospital twenty-nine days. *Postoperative history*—great improvement; recurrent attacks of indigestion.

Gyn. No. 2108. March 19, 1907. Aged fifty-four years. *Symptoms*—colic, two years; jaundice; vomiting; pain lower abdomen; bloody vaginal discharge. *Clinical diagnosis*—cholelithiasis; multiple fibroids. *Pathological diagnosis*—fibromyoma uteri; gall-stones. *Operation*—cholecystotomy; hysterectomy; bilateral salpingo-oöphorectomy. *Convalescence*—normal; in hospital thirty-nine days. *Postoperative history*—complete cure.

Gyn. No. 2218. July 1, 1907. Aged twenty-two years. *Symptoms*—colic, three and one-half years; vomiting; bearing down pains; cramps before menstruation. *Clinical diagnosis*—R. V. O.;

retroversion; cholelithiasis; fibromyoma of rectus muscle. *Pathological diagnosis*—fibromyoma rectus abdominalis; gall-stone. *Operation*—cholecystotomy; plastic; suspension. *Convalescence*—phlebitis of femoral vein; feverish convalescence; poor drainage; persistent sinus; in hospital thirty-eight days. *Postoperative history*—not traced.

Gyn. No. 2349. November 27, 1907. Aged fifty-six years. *Symptoms*—nausea and vomiting after meals for seven weeks; pain in abdomen; intense prostration. *Clinical diagnosis*—umbilical hernia; cholelithiasis. *Operation*—cholelithotomy; herniorrhaphy. *Convalescence*—stupor and death; in hospital eleven days. *Postoperative history*—died from cholemia.

Gyn. No. 2518. April 20, 1908. Aged thirty-five years. *Symptoms*—backache; indigestion, one year; pain in epigastrium; vomiting; jaundice; colic; clay stools. *Clinical diagnosis*—right dermoid cyst; hematoma left ovary; cholelithiasis. *Pathological diagnosis*—ovarian teratoma; gall-stones. *Operation*—cholecystotomy; right salpingo-oöphorectomy. *Convalescence*—patient pulled drainage-tube out second day; no harmful result; postoperative fever; in hospital thirty-three days. *Postoperative history*—complete cure.

Gyn. No. 2737. November 19, 1908. Aged twenty-eight years. *Symptoms*—vaginal bleeding, one week; colic two weeks. *Clinical diagnosis*—endometritis; salpingitis; appendicitis; retroversion; cholelithiasis. *Pathological diagnosis*—periappendicitis; interstitial endometritis; hydrosalpinx; gall-stones. *Operation*—cholecystotomy; appendectomy; suspension; right salpingectomy. *Convalescence*—normal; in hospital twenty-seven days. *Postoperative history*—complete cure.

Gyn. No. 2394. January 21, 1908. Aged forty-five years. *Symptoms*—fulness after eating; tenderness after eating; jaundice. *Clinical diagnosis*—retroversion; chronic cholecystitis; R. V. O. *Pathological diagnosis*—catarrhal salpingitis; salpingo-oöphoritis. *Operation*—cholecystotomy; ventrosuspension; salpingo-oöphorectomy, right. *Convalescence*—poor drainage and fever; in hospital twenty-nine days. *Postoperative history* (see Case No. 2940). Returned for second operation.

Gyn. No. 2467. March 12, 1908. Aged forty-five years. *Symptoms*—indigestion; constipation; burning and frequency of urination; abdominal pain. *Clinical diagnosis*—dermoid cyst; cholelithiasis. *Pathological diagnosis*—teratoma of left ovary; bilateral peri-salpingitis; obliterative appendicitis and gall-stones. *Operation*—cholecystotomy; appendectomy; bilateral salpingo-oöphorectomy. *Convalescence*—normal; in hospital thirty-two days. *Postoperative history*—not traced.

Gyn. No. 2790. January 14, 1909. Aged thirty years. *Symptoms*—colic, five months; jaundice; vomiting; ventral hernia. *Clinical diagnosis*—cholelithiasis; umbilical hernia. *Pathological*

diagnosis—gall-stones. *Operation*—cholecystostomy; herniotomy. *Convalescence*—conjunctivitis; in hospital thirty-four days. *Postoperative history*—complete cure.

Gyn. No. 2316. January 31, 1909. Aged thirty-nine years. *Symptoms*—dysmenorrhea; pain in right iliac region; slight on left side; indigestion; pain in epigastrium. *Clinical diagnosis*—R. V. O.; diastasis recti; cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—plastic; appendectomy; cholecystostomy; Webster operation. *Convalescence*—persistent sinus; in hospital sixty-six days. *Postoperative history*—for two years after operation had almost constant hemorrhage from stomach with occasional jaundice; during past two years has regained health.

Gyn. No. 2853. March 4, 1909. Aged thirty-seven years. *Symptoms*—indigestion for five weeks; swelling in right side for one month. *Clinical diagnosis*—uterine fibroid; pregnancy; cholelithiasis. *Pathological diagnosis*—fibromyoma; uteri; fetus; gall-stones. *Operation*—myomectomy; Cesarean section; cholecystostomy. *Convalescence*—wound abscess; in hospital thirty-eight days. *Postoperative history*—complete cure.

Gyn. No. 2864 $\frac{1}{2}$. March 29, 1909. Aged forty-six years. *Symptoms*—pain in epigastrium and right hypochondrium, three months; jaundice; flatulence; bleeding from vagina. *Clinical diagnosis*—uterine fibroid; cholelithiasis. *Pathological diagnosis*—glandular endometritis; right tubo-ovarian cyst; left hydrosalpinx; gall-stones. *Operation*—hysterectomy; bilateral salpingo-oophorectomy; cholecystostomy. *Convalescence*—pneumonia; in hospital twenty-nine days. *Postoperative history*—readmitted (see Case No. 3961).

Gyn. No. 2864 $\frac{3}{4}$. April 4, 1909. Aged thirty-six years. *Symptoms*—flatulence; abdominal distress; sleeplessness; indigestion. *Clinical diagnosis*—cholelithiasis; pelvic adhesions. *Pathological diagnosis*—left hydrosalpinx; perioöphoritis; normal appendix; gall-stones. *Operation*—cholecystostomy; left salpingo-oophorectomy. *Convalescence*—normal; in hospital thirty-five days. *Postoperative history*—marked improvement; still complains of indigestion.

Gyn. No. 2886. April 6, 1909. Aged fifty-four years. *Symptoms*—uterine hemorrhage, five years; indigestion, ten years. *Clinical diagnosis*—uterine fibroid; cholelithiasis; hydrosalpinx. *Pathological diagnosis*—fibromyoma uteri; right parovarian cyst; chronic cholecystitis; normal ovaries; gall-stones. *Operation*—hysterectomy; bilateral salpingo-oophorectomy; appendectomy; cholecystectomy. *Convalescence*—normal; in hospital twenty-eight days. *Postoperative history*—postoperative insanity for six months, followed by complete recovery.

Gyn. No. 3019. July 2, 1909. Aged fifty-five years. *Symptoms*—abdominal pain for fifteen months. *Clinical diagnosis*—cholelithiasis; R. V. O. *Pathological diagnosis*—gall-stones. *Opera-*

tion—plastic; cholecystostomy. *Convalescence*—normal; in hospital twenty-eight days. *Postoperative history*—patient well until July, 1911, when after a serious fall developed pain in abdomen; laparotomy performed and intestinal adhesions found; died post-operative pneumonia.

Gyn. No. 3104. November 7, 1909. Aged forty-nine years. *Symptoms*—pain in right ovarian region and right side; abdominal enlargement; menorrhagia; frequency of urination; constipated; indigestion. *Clinical diagnosis*—uterine fibroid; chronic appendicitis; cholelithiasis; intestinal adhesions. *Pathological diagnosis*—fibromyoma uteri; periappendicitis; follicular cyst of left ovary. *Operation*—hysterectomy; appendectomy; bilateral salpingectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-four days. *Postoperative history*—cured except for constipation and hemorrhoids.

Gyn. No. 3121. November 22, 1909. *Symptoms*—irregular bleeding from vagina; indigestion; flatulence; intensely neurotic. *Clinical diagnosis*—carcinoma of fundus; cholelithiasis. *Pathological diagnosis*—adenocarcinoma corporis uteri; gall-stones. *Operation*—hysterectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-seven days. *Postoperative history*—relief of all symptoms; still neurotic.

Gyn. No. 3181. January 27, 1910. Aged thirty-four years. *Symptoms*—pain and tenderness in region of umbilicus and gall-bladder. *Clinical diagnosis*—umbilical hernia; diastasis recti; cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystostomy; herniorrhaphy; Webster operation. *Convalescence*—normal; in hospital twenty-five days. *Postoperative history*—complete cure.

Gyn. No. 3186½. February 2, 1910. Aged forty-three years. *Symptoms*—dragging pain in pelvis; backache; colic, eighteen years; jaundice; vomiting. *Clinical diagnosis*—R. V. O.; cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—plastic; cholecystostomy. *Convalescence*—normal; in hospital nineteen days. *Postoperative history*—not traced.

Gyn. No. 3194. February 8, 1910. Aged forty-one years. *Symptoms*—menorrhagia; leukorrhea; colic, many years; tenderness over gall-bladder. *Clinical diagnosis*—R. V. O.; lacerated cervix; chronic metritis; cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—plastic; cholecystostomy. *Convalescence*—normal; in hospital twenty-three days. *Postoperative history*—complete cure.

Gyn. No. 3211. February 23, 1910. Aged forty-nine years. *Symptoms*—vomiting; jaundice; colic for six months; constipation; gastric irritability; menorrhagia; malodorous leukorrhea; clay-colored stools. *Clinical diagnosis*—fibroma uteri; cholelithiasis. *Pathological diagnosis*—fibroma uteri; left hydrosalpinx; chronic cholecystitis; gall-stones; right perisalpingitis; right perioöphoritis.

Operation—hysterectomy; bilateral salpingo-oöphorectomy; cholecystectomy. *Convalescence*—normal; in hospital forty days. *Postoperative history*—complete cure except one attack of pain in upper abdomen of short duration.

Gyn. No. 3252. March 24, 1910. Aged thirty-eight years. *Symptoms*—metrorrhagia; pain in umbilicus. *Clinical diagnosis*—lacerated cervix; cholelithiasis. *Pathological diagnosis*—concretion in appendix; gall-stones. *Operation*—plastic; appendectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-four days. *Postoperative history*—no improvement; operation in another hospital.

Gyn. No. 3331. May 28, 1910. Aged forty years. *Symptoms*—indigestion, two years; pain in right hypochondrium; epigastric pain after eating; vomiting. *Clinical diagnosis*—cholelithiasis; cecum mobile. *Pathological diagnosis*—normal appendix; gall-stones. *Operation*—cholecystostomy; appendectomy. *Convalescence*—normal; in hospital twenty-four days. *Postoperative history*—complete cure.

Gyn. No. 3349. June 12, 1910. Aged forty-two years. *Symptoms*—pain in right inguinal region; menorrhagia; constipation; vesical irritability; colic for years; vomiting. *Clinical diagnosis*—myoma uteri; cholelithiasis. *Pathological diagnosis*—adenomyoma uteri; fibromyoma uteri; right catarrhal salpingitis; left hydrosalpinx; periappendicitis. *Operation*—hysterectomy; appendectomy; cholecystostomy. *Convalescence*—hematoma in wound; pelvic cellulitis; vesical irritability; in hospital thirty-eight days. *Postoperative history*—marked improvement; suffers at times with hyperacidity.

Gyn. No. 3407. August 29, 1910. Aged thirty-two years. *Symptoms*—not given. *Clinical diagnosis*—appendicitis; gall-stones; right ovarian cyst. *Pathological diagnosis*—right cystic ovary; gall-stones. *Operation*—right oöphorectomy; appendectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-two days. *Postoperative history*—not traced.

Gyn. No. 3445. September 26, 1910. Aged twenty-eight years. *Symptoms*—"bilious attacks" many years; vomiting; colic, one year. *Clinical diagnosis*—chronic cholecystitis; chronic appendicitis. *Pathological diagnosis*—chronic appendicitis. *Operation*—cholecystostomy; appendectomy. *Convalescence*—normal; in hospital twenty-two days. *Postoperative history*—returned for second operation (see Case No. 3991).

Gyn. No. 3539. November 29, 1910. Aged forty-nine years. *Symptoms*—pain in back; leucorrhea, four months; pain in legs; loss in weight; recurrent epigastric pain. *Clinical diagnosis*—fibroid of uterus; cholecystitis; cholelithiasis; retrocecal appendix; kink of sigmoid. *Pathological diagnosis*—fibromyoma uteri; periappendicitis; gall-stones. *Operation*—hysterectomy; appendec-

tomy; bilateral salpingo-oöphorectomy; cholecystostomy. *Convalescence*—normal; in hospital thirty-six days. *Postoperative history*—complete cure.

Gyn. No. 3511. November 2, 1910. Aged fifty-four years. *Symptoms*—backache; pain in both legs; hunger pain in right hypochondrium; flatulence. *Clinical diagnosis*—cholelithiasis. *Operation*—cholecystectomy; appendectomy. *Convalescence*—temperature $102\frac{2}{5}^{\circ}$ F. seventh day. Thereafter normal; in hospital twenty-six days. *Postoperative history*—complete cure.

Gyn. No. 3666. March 19, 1911. Aged twenty-four years. *Symptoms*—appendiceal colic, three and one-half years; gall-bladder colic, one and one-half years; vomiting; constipation. *Clinical diagnosis*—appendicitis. *Pathological diagnosis*—normal appendix. *Operation*—appendectomy; cholecystostomy. *Convalescence*—discharge with drain in gall-bladder; normal convalescence; in hospital twenty-four days. *Postoperative history*—(see Case No. 3758). Returned for second operation.

Gyn. No. 3940. November 21, 1911. Aged forty-three years. *Symptoms*—dysmenorrhea, four years; colic, four years; vomiting; flatulence; constipation; jaundice. *Clinical diagnosis*—cholecystitis; pelvic inflammatory disease. *Pathological diagnosis*—fibromyoma uteri; bilateral pyosalpinx. *Operation*—hysterectomy; bilateral salpingo-oöphorectomy; cholecystotomy. *Convalescence*—normal; in hospital twenty-six days. *Postoperative history*—not traced.

Gyn. No. 3963. November 14, 1911. Aged forty-two years. *Symptoms*—dragging pain in lower abdomen; frequent urination; colic two years. *Clinical diagnosis*—R. V. O.; retroflexion; cholelithiasis. *Pathological diagnosis*—chronic cholecystitis; obliterative appendicitis. *Operation*—Plastic; suspension; appendectomy; cholecystectomy. *Convalescence*—normal; in hospital twenty-two days. *Postoperative history*—great improvement; complained of heaviness in stomach and heart-burn; limited diet.

Gyn. No. 3995. December 9, 1911. Aged thirty-five years. *Symptoms*—backache; headache; mass in vagina; dragging pain; colic once. *Clinical diagnosis*—R. V. O.; retroflexion; cholelithiasis. *Pathological diagnosis*—gall-stone. *Operation*—plastic; suspension; cholecystostomy. *Convalescence*—normal; in hospital twenty-four days. *Postoperative history*—small hernia developed in gall-bladder scar with keloid formation, requiring repair; complete relief of original symptoms.

Gyn. No. 4007. December 20, 1911. Aged twenty-eight years. *Symptoms*—pain in left lower and upper abdomen; vomiting. *Clinical diagnosis*—cholelithiasis; left cystic ovary; diastasis recti. *Pathological diagnosis*—left catarrhal salpingitis; normal appendix; gall-stones. *Operation*—left salpingo-oöphorectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-six days. *Post-*

operative history—much better since operation; some discomfort in epigastrium.

Gyn. No. 4023. January 5, 1912. Aged twenty-seven years. *Symptoms*—colic, one and one-half years; vomiting. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—obliterative appendicitis; gall-stones. *Operation*—cholecystenterostomy appendectomy. *Convalescence*—normal; in hospital nineteen days. *Post-operative history*—cured; occasional attack of backache.

Gyn. No. 4048. January 16, 1912. Aged thirty-seven years. *Symptoms*—leucorrhea; dysmenorrhea; severe headache; nausea; jaundice; gastric distress; frequency and urgency of urination. *Clinical diagnosis*—R. V. O.; lacerated cervix; cholelithiasis. *Pathological diagnosis*—erosion of cervix; gall-stone. *Operation*—plastic; ligation of ovarian veins; cholecystostomy. *Convalescence*—normal; in hospital twenty-one days. *Postoperative history*—complete cure except recurrence of headache.

Gyn. No. 4050. January 18, 1912. Aged forty-nine years. *Symptoms*—nervous indigestion, thirty years; colic; vomiting; jaundice; clay-colored stools; dark urine; prolapsus. *Clinical diagnosis*—R. V. O.; cholelithiasis. *Pathological diagnosis*—chronic cholecystitis; gall-stone. *Operation*—plastic; partial cholecystectomy; choledochotomy. *Convalescence*—diaphragmatic pleurisy; sinus on discharge; in hospital thirty-two days. *Post-operative history*—complete cure.

Gyn. No. 4071. February 5, 1912. Aged forty-five years. *Symptoms*—indigestion; flatulence; nausea; leucorrhea; pain lower abdomen. *Clinical diagnosis*—cholelithiasis; chronic appendicitis; retroflexion. *Pathological diagnosis*—chronic appendicitis. *Operation*—suspension; appendectomy; cholecystostomy. *Postoperative history*—complete cure.

Gyn. No. 4089. February 15, 1912. Aged fifty-two years. *Symptoms*—frequency of urination; constipation; abdominal tumor; bleeding from vagina; colic for three years; jaundice. *Clinical diagnosis*—cholelithiasis; ovarian cysts; myoma uteri (carcinoma). *Pathological diagnosis*—adenocarcinoma left ovary; bilateral perisalpingitis; gall-stones. *Operation*—panhysterectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-one days. *Post-operative history*—complete cure.

Gyn. No. 4171. April 20, 1912. Aged fifty-one years. *Symptoms*—vomiting after meals, nine years; severe pain over gall-bladder, one year; loss of weight. *Clinical diagnosis*—cholelithiasis; chronic pancreatitis; ventral hernia. *Operation*—cholecystostomy; herniorrhaphy. *Convalescence*—continued vomiting; in hospital twenty-two days; gradual asthenia; died of cholemia.

Gyn. No. 4179. April 25, 1912. Aged forty-three years. *Symptoms*—headache; numbness in thighs; pain over coccyx; acute indigestion for years; flatulence. *Clinical diagnosis*—retroflexion;

cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—plastic; suspension; cholecystostomy. *Convalescence*—normal; in hospital twenty-two days. *Postoperative history*—complete relief except slight backache; no gall-bladder symptoms.

Gyn. No. 4217. May 14, 1912. Aged forty-two years. *Symptoms*—menorrhagia; frequency of urination; heart-burn; pain in right hypochondrium. *Clinical diagnosis*—myoma uteri; cholelithiasis. *Pathological diagnosis*—fibromyoma uteri; gall-stones. *Operation*—hysteromyomectomy; cholecystostomy. *Convalescence*—superficial wound infection; in hospital twenty-four days. *Postoperative history*—complete cure.

Gyn. No. 4218. May 17, 1912. Aged fifty-two years. *Symptoms*—pain in right hypochondrium, one year; frequency of urination. *Clinical diagnosis*—cholecystitis; intestinal adhesions. *Pathological diagnosis*—chronic cholecystitis; peri-appendicitis. *Operation*—appendectomy; cholecystectomy. *Convalescence*—normal; in hospital twenty-six days. *Postoperative history*—not improved; has continuous pain in gall-bladder region.

Gyn. No. 4232. May 27, 1912. Aged forty-three years. *Symptoms*—colic, twenty years; nausea; flatulence; pain in left lower abdomen. *Clinical diagnosis*—myoma uteri; chronic cholecystitis. *Pathological diagnosis*—fibromyoma uteri; left perisalpingo-oöphoritis; normal appendix. *Operation*—hysterectomy; left salpingo-oöphorectomy; appendectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-three days. *Postoperative history*—great improvement; occasional attack of pain in gall-bladder region; constipation.

Gyn. No. 4241. June 6, 1912. Aged thirty-five years. *Symptoms*—pain in right lower abdomen; worse before period; colic for three years. *Clinical diagnosis*—chronic cholecystitis; bilateral hydrosalpinx. *Pathological diagnosis*—fibro-myoma uteri; bilateral hydrosalpinx; normal appendix. *Operation*—cholecystostomy; appendectomy; bilateral salpingectomy. *Convalescence*—normal; in hospital twenty-three days. *Postoperative history*—complete cure.

Gyn. No. 4243. June 7, 1912. *Symptoms*—emphyema of gall-bladder following typhoid fever. *Clinical diagnosis*—emphyema of gall-bladder; cholelithiasis; acute appendicitis. *Operation*—cholecystostomy; appendectomy. *Convalescence*—normal; in hospital twenty-three days. *Postoperative history*—slight improvement after operation; recurrence of pain in gall-bladder region. flatulence; nausea; vomiting; headache; constipation; second operation twenty months later; cystic duct was found completely occluded; gall-bladder was chronically inflamed and pyloric adhesions were present; cholecystectomy and adhesions released, March 18, 1914.

Gyn. No. 4264. July 3, 1912. Aged thirty-one years. *Symptoms*—pain in lower abdomen; headache; colic, seven years; vomiting; leucorrhea; fatigue. *Clinical diagnosis*—cholelithiasis; empyema of gall-bladder; retroflexion; R. V. O. *Pathological diagnosis*—chronic cholecystitis; obliterative appendicitis; gall-stones. *Operation*—plastic; suspension; appendectomy; cholecystectomy. *Convalescence*—normal; twenty-five days. *Postoperative history*—complete recovery so far as upper abdomen is concerned; still has menorrhagia.

Gyn. No. 4295. August 12, 1912. Aged twenty-eight years. *Symptoms*—pain in right hypochondrium; vomiting; colic, one year; chills. *Clinical diagnosis*—cholelithiasis; chronic cholecystitis; perineovaginal fistula. *Pathological diagnosis*—chronic cholecystitis; gall-stones; normal appendix. *Operation*—plastic; appendectomy; cholecystectomy. *Convalescence*—normal; in hospital seventeen days. *Postoperative history*—complete cure except for slight pain and fulness in epigastrium.

Gyn. No. 4306. August 19, 1912. Aged fifty-three years. *Symptoms*—general abdominal colic, six months; nausea and burning in epigastrium; jaundice; no local pain. *Clinical diagnosis*—cholelithiasis; mucocele of appendix. *Pathological diagnosis*—chronic cholecystitis; gall-stones; mucocele of appendix. *Operation*—cholecystectomy; appendectomy. *Convalescence*—phlebitis and thrombosis of left femoral vein; in hospital forty days. *Postoperative history*—complete cure.

Gyn. No. 4310. August 20, 1912. Aged thirty-nine years. *Symptoms*—backache; frequency of urination; colic one and one-half years. *Clinical diagnosis*—R. V. O.; cystocele; cholelithiasis. *Operation*—plastic; appendectomy; cholecystostomy. *Convalescence*—superficial wound infection; small sinus on discharge; in hospital fifty-six days. *Postoperative history*—cured; has neurasthenic symptoms.

Gyn. No. 4372. October 4, 1912. Aged twenty-seven years. *Symptoms*—indigestion, eight years; diarrhea; colic, six months; vomiting. *Clinical diagnosis*—cholelithiasis. *Pathological diagnosis*—obliterative appendicitis; gall-stones. *Operation*—cholecystostomy; appendectomy. *Convalescence*—normal; in hospital fifteen days. *Postoperative history*—complete cure.

Gyn. No. 4412. October 24, 1912. Aged thirty-eight years. *Symptoms*—colic, six years; dragging pain in back. *Clinical diagnosis*—R. V. O.; retroflexion; cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystostomy; plastic; suspension. *Convalescence*—normal; in hospital twenty-one days; *Postoperative history*—not traced.

Gyn. No. 4416. October 27, 1912. Aged forty-three years. *Symptoms*—proidentia uteri; dragging pain; constant pain in lower abdomen; occasional epigastric distress after meals. *Clinical*

diagnosis—R. V. O.; chronic appendicitis; retroversion; cholelithiasis. *Pathological diagnosis*—chronic appendicitis; gall-stones. *Operation*—cholecystotomy; plastic; suspension; appendectomy. *Convalescence*—slight fever; in hospital nineteen days. *Postoperative history*—recurrence of prolapsus; suffers greatly with indigestion.

Gyn. No. 4460. November 18, 1912. Aged fifty-four years. *Symptoms*—indigestion for eight years; left-sided pain; colic for five weeks. *Clinical diagnosis*—myoma uteri; right salpingo-oöphoritis; cholelithiasis. *Pathological diagnosis*—fibromyoma uteri; right tubo-ovarian cyst; gall-stones. *Operation*—hysterectomy; conservation of left ovary; cholecystostomy. *Convalescence*—one attack of colic on twentieth day; in hospital twenty-four days. *Postoperative history*—complete cure; has slight menopausal symptoms.

Gyn. No. 4538. January 12, 1913. *Symptoms*—upper abdominal distress for two years. *Clinical diagnosis*—R. V. O.; retroflexion; cholelithiasis. *Pathological diagnosis*—gall-stone. *Operation*—cholecystostomy; plastic; suspension. *Convalescence*—normal; in hospital twenty-one days. *Postoperative history*—slight improvement; recurrence of colicky pains.

Gyn. No. 4559. January 5, 1913. Aged twenty-two years. *Symptoms*—menorrhagia; lower abdominal soreness; obstinate constipation; "weak stomach;" colic once. *Clinical diagnosis*—retroflexion; cirrhotic ovaries; cholelithiasis. *Pathological diagnosis*—chronic cholecystitis; gall-stones. *Operation*—suspension; cauterization of ovaries; cholecystectomy. *Convalescence*—superficial wound infection; in hospital twenty-nine days. *Postoperative history*—returned March 13, 1913, complaining of profuse vaginal discharge and persistent gastric irritability; exceedingly hysterical; no operation.

Gyn. No. 4570. January 31, 1913. Aged twenty-eight years. *Symptoms*—pain after eating, three years; severe colic with jaundice, six months ago. *Clinical diagnosis*—cholecystitis. *Operation*—cholecystotomy; plastic. *Convalescence*—septic temperature; abscess evacuated through wound on twenty-seventh day; death thirty-first day.

Gyn. No. 4581. February 11, 1913. Aged fifty years. *Symptoms*—irregular, profuse menstruation; indigestion; flatulence; epigastric pain. *Clinical diagnosis*—multiple fibroids; cholelithiasis; adherent appendix. *Pathological diagnosis*—myoma uteri; bilateral pyosalpinx; peri-appendicitis; cholecystitis; gall-stones. *Operation*—hysterectomy; bilateral salpingo-oöphorectomy; appendectomy; cholecystectomy. *Convalescence*—wound infection; sinus on discharge; in hospital thirty-eight days. *Postoperative history*—great improvement; flatulence; pain over incision; symptoms of menopause.

Gyn. No. 4582. January 11, 1913. Aged forty years. *Symptoms*—flatulence and nausea, one year; soreness in epigastrium. *Clinical diagnosis*—cholelithiasis; floating kidney. *Pathological diagnosis*—gall-stones. *Operation*—cholecystostomy; nephropexy. *Convalescence*—normal; in hospital twenty-eight days. *Postoperative history*—general improvement excellent; slight indigestion.

Gyn. No. 4655. April 5, 1913. Aged thirty-nine years. *Symptoms*—dull pain in right lower abdomen; poor appetite; indigestion. *Clinical diagnosis*—subacute appendicitis; chronic metritis; cholelithiasis. *Pathological diagnosis*—myometritis; obliterative appendicitis; chronic cholecystitis. *Operation*—hysterectomy; bilateral salpingectomy; appendectomy; cholecystectomy. *Convalescence*—peritonitis; death fourteenth day.

Gyn. No. 4696. April 30, 1913. Aged thirty-six years. *Symptoms*—pain in lower abdomen and epigastrium; nausea. *Clinical diagnosis*—R. V. O.; retroflexion; cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—plastic; suspension; cholecystostomy. *Convalescence*—normal; in hospital twenty-six days. *Postoperative history*—complete relief of pain in epigastrium; complains of constipation.

Gyn. No. 4808. July 13, 1913. Aged forty years. *Symptoms*—colic, five months; constipation; heartburn; loss in weight. *Clinical diagnosis*—cholelithiasis; adherent appendix. *Pathological diagnosis*—chronic appendicitis; gall-stones. *Operation*—cholecystostomy; appendectomy. *Convalescence*—old tubercular process in lung became active; sinus on discharge; in hospital twenty-four days. *Postoperative history*—complete cure.

COMBINED OPERATIONS WITHOUT GALL-BLADDER SYMPTOMS.

Gyn. No. 917. May 21, 1903. Aged sixty years. *Symptoms*—dysuria; weakness and malnutrition. *Clinical diagnosis*—twisted ovarian cyst; cholelithiasis. *Pathological diagnosis*—bilateral papillomatous cysts of ovaries. *Operation*—cholelithotomy; hysterosalpingo-oöphorectomy. *Convalescence*—normal; in hospital forty-nine days. *Postoperative history*—well for several years; died ten years after operation; cause unknown.

Gyn. 1055. October 17, 1903. Aged thirty-five years. *Symptoms*—pain in right iliac region; backache; constipation. *Clinical diagnosis*—retroversion; adherent appendix; cholelithiasis; right parovarian cyst. *Pathological diagnosis*—parovarian cyst; gall-stones. *Operation*—appendectomy; cholelithotomy; right cystectomy; suspension. *Convalescence*—normal; in hospital twenty-eight days. *Postoperative history*—two years later had gall-bladder pain for one year; now complete cure.

Gyn. No 1061. October 21, 1903. Aged forty-three years. *Symptoms*—abdominal heaviness and enlargement. *Clinical diag-*

nosis—fibroid of uterus; cholelithiasis. *Pathological diagnosis*—fibro-myoma uteri; atrophic endometritis; *Operation*—cholelithotomy; supravaginal hysterectomy; right ovary conserved. *Convalescence*—suppuration of cervical stump; in hospital forty-eight days. *Postoperative history*—complete cure; except for slight pain in gall-bladder incision.

Gyn. No. 1071. November 9, 1903. Aged forty-five years. *Symptoms*—abdominal cyst. *Clinical diagnosis*—right multilocular ovarian cyst; cholelithiasis; intestinal adhesions. *Pathological diagnosis*—cystadenoma ovarii; pseudomucinosum glandulare. *Operation*—cholelithotomy; ventrofixation; salpingo-oöphorectomy. *Convalescence*—urinary retention; cystitis; in hospital twenty-eight days. *Postoperative history*—not traced.

Gyn. No. 1181. March 9, 1904. Aged fifty years. *Symptoms*—metrorrhagia; menorrhagia; backache; incontinence of urine. *Clinical diagnosis*—uterine fibroid; cholelithiasis. *Pathological diagnosis*—fibromyoma uteri; atrophic endometritis; gall-stones. *Operation*—hysterectomy; cholelithotomy. *Convalescence*—pain in chest with slight fever; in hospital thirty-one days. *Postoperative history*—complete cure with exception of occasional headache.

Gyn. No. 1840. June 5, 1906. Aged forty-eight years. *Symptoms*—menorrhagia; pain in lower abdomen referred down right leg. *Clinical diagnosis*—sloughing submucous fibroid; cholelithiasis. *Pathological diagnosis*—myoma uteri; chronic oöphoritis; gall-stones. *Operation*—panhysterectomy; cholelithotomy. *Convalescence*—normal; in hospital thirty-seven days. *Postoperative history*—not traced.

Gyn. No. 1963. October 18, 1906. Aged thirty-six years. *Symptoms*—pain in back, shooting down thighs; cold feet; tingling; frequency of urination; menorrhagia. *Clinical diagnosis*—uterine fibroid; cholelithiasis. *Pathological diagnosis*—fibromyoma uteri; gall-stones. *Operation*—hysterectomy; conservation of right ovary; cholelithotomy. *Convalescence*—superficial wound infection; in hospital twenty-five days. *Postoperative history*—complete cure.

Gyn. No. 2029. January 3, 1907. Aged fifty-one years. *Symptoms*—prolapsus. *Clinical diagnosis*—complete prolapsus; R. V. O. *Pathological diagnosis*—hypertrophied cervix. *Operation*—cholecystotomy; plastic; fixation of uterus. *Convalescence*—normal; in hospital thirty-three days. *Postoperative history*—not traced.

Gyn. No. 2162. May 12, 1907. Aged thirty-five years. *Symptoms*—not given. *Clinical diagnosis*—retroflexion; R. V. O.; lacerated cervix. *Operation*—cholecystotomy; plastic; suspension. *Convalescence*—normal; in hospital twenty-two days. *Postoperative history*—not traced.

Gyn. No. 2670. October 6, 1908. Aged thirty-nine years. *Symptoms*—dysuria; frequency of urination. *Clinical diagnosis*—myoma uteri; cholelithiasis. *Pathological diagnosis*—fibromyoma

uteri; glandular endometritis; follicular cyst left ovary, cholecystitis. *Operation*—hysterectomy; conservation right ovary; cholecystectomy. *Convalescence*—slight prolongation of vomiting; in hospital twenty-three days. *Postoperative history*—complete cure.

Gyn. No. 2447. February 28, 1908. Aged fifty-two years. *Symptoms*—hernia in left groin; backache; leucorrhea. *Clinical diagnosis*—R. V. O.; retroversion; femoral hernia; cholelithiasis. *Pathological diagnosis*—gall-stones. *Operation*—cholecystotomy; plastic; suspension; herniorrhaphy. *Convalescence*—normal; in hospital twenty-seven days. *Postoperative history*—complete recovery.

Gyn. No. 2757. December 5, 1908. Aged forty-one years. *Symptoms*—pain in rectum and on micturition; abdominal tumor. *Clinical diagnosis*—myoma uteri; cholelithiasis. *Pathological diagnosis*—fibromyoma uteri; gall-stones. *Operation*—hysterectomy; conservation right ovary; cholecystostomy. *Convalescence*—persistent abdominal pain, especially on right side; in hospital forty-five days. *Postoperative history*—not traced.

Gyn. No. 2988. June 21, 1909. Aged sixty-five years. *Symptoms*—bleeding from vagina, two months. *Clinical diagnosis*—myoma uteri; cholelithiasis. *Pathological diagnosis*—fibromyoma uteri; bilateral pyosalpinx; perioöphoritis; gall-stones. *Operation*—cholelithotomy; hysterectomy; bilateral salpingo-oöphorectomy. *Convalescence*—phlebitis of right leg; in hospital twenty-one days. *Postoperative history*—complete cure.

Gyn. No. 3046. September 14, 1909. Aged sixty years. *Symptoms*—swelling of abdomen and pain. *Clinical diagnosis*—multilocular ovarian cyst; cholelithiasis. *Pathological diagnosis*—cystadenoma ovarii pseudomucinosum glandulare; gall-stones. *Operation*—salpingo-oöphorectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-nine days. *Postoperative history*—complete physical recovery; five years later mind affected.

Gyn. No. 3587. January 11, 1911. Aged forty-eight years. *Symptoms*—menorrhagia; metrorrhagia. *Clinical diagnosis*—retroflexion; cholelithiasis. *Pathological diagnosis*—interstitial endometritis; gall-stones. *Operation*—hysterectomy; salpingo-oöphorectomy; appendectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-six days. *Postoperative history*—not traced.

Gyn. No. 3632. February 16, 1911. Aged forty-two years. *Symptoms*—not given. *Clinical diagnosis*—umbilical hernia; cholelithiasis; hemorrhoids. *Pathological diagnosis*—gall-stones. *Operation*—plastic; herniorrhaphy; cholecystostomy. *Convalescence*—normal; in hospital twenty-one days. *Postoperative history*—complete cure.

Gyn. No. 3707. April 19, 1911. Aged forty-three years. *Symptoms*—constipation. *Clinical diagnosis*—tubo-ovarian cyst; mucoid

appendix; cholelithiasis. *Pathological diagnosis*—chronic metritis; bilateral pyosalpinx; catarrhal appendix; gall-stone. *Operation*—hysterectomy; bilateral salpingo-oöphorectomy; appendectomy; cholecystostomy. *Convalescence*—normal; in hospital nineteen days. *Postoperative history*—gastric condition excellent; slight pain in gall-bladder incision; needs light laxative; has menopausal symptoms.

Gyn. No. 3764. June 2, 1911. Aged twenty-six years. *Symptoms*—pain in lower abdomen and sacrum; headache; menorrhagia. *Clinical diagnosis*—R. V. O.; lacerated cervix; retroflexion; appendicitis; cholelithiasis. *Pathological diagnosis*—endometritis cervicis; peri-appendicitis; gall-stones. *Operation*—plastic; appendectomy; suspension; cholecystostomy. *Convalescence*—normal; in hospital twenty-two days. *Postoperative history*—not traced.

Gyn. No. 3771. June 11, 1911. Aged forty-nine years. *Symptoms*—menorrhagia. *Clinical diagnosis*—uterine fibroid; cholelithiasis. *Pathological diagnosis*—fibromyoma uteri; bilateral pyosalpinx; gall-stones. *Operation*—hysterectomy; bilateral salpingo-oöphorectomy; cholecystostomy. *Convalescence*—normal in hospital twenty-three days. *Postoperative history*—complete cure.

Gyn. No. 3811. July 22, 1911. Aged thirty-two years. *Symptoms*—pain lower abdomen; heaviness; several attacks of appendicitis. *Clinical diagnosis*—R. V. O.; retroversion; cholelithiasis; right cystic ovary; chronic appendicitis; hemorrhoids. *Pathological diagnosis*—chronic appendicitis; gall-stone. *Operation*—cholecystostomy; appendectomy; suspension; plastic; right oöphorectomy. *Convalescence*—normal; twenty-nine days. *Postoperative history*—no upper abdominal symptoms. Intense menorrhagia.

Gyn. No. 3837. August 15, 1911. Aged thirty years. *Symptoms*—sharp pain both sides of lower abdomen; leucorrhea. *Clinical diagnosis*—R. V. O.; retroflexion; cholelithiasis. *Pathological diagnosis*—chronic cholelithiasis; gall-stones. *Operation*—cholecystectomy; plastic; suspension. *Convalescence*—normal; in hospital twenty-five days. *Postoperative history*—no improvement; worse than before operation.

Gyn. No. 3983. December 2, 1911. Aged forty-four years. *Symptoms*—backache; headache; dragging pain in pelvis; menorrhagia. *Clinical diagnosis*—chronic metritis; cholelithiasis. *Pathological diagnosis*—adenomyoma uteri; bilateral catarrhal salpingitis; normal appendix; gall-stones. *Operation*—hysterectomy; bilateral salpingectomy; appendectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-two days. *Postoperative history*—no upper abdominal symptoms; patient is nervous and complains of pain in left side and rectum.

Gyn. No. 4037. January 10, 1912. Aged thirty-four years. *Symptoms*—dull pain in right lower abdomen with swelling;

menorrhagia; constipation. *Clinical diagnosis*—uterine fibroid; cholecystitis; cholelithiasis. *Pathological diagnosis*—fibromyoma uteri; bilateral perisalpingitis; gall-stones. *Operation*—hysterectomy; bilateral salpingectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-one days. *Postoperative history*—complete cure.

Gyn. No. 4043. January 13, 1912. Aged thirty-three years. *Symptoms*—pain in lower right abdomen, one year; acute pain daily in this region. *Clinical diagnosis*—R. V. O.; chronic appendicitis; cholecystitis. *Pathological diagnosis*—normal appendix. *Operation*—plastic; appendectomy; cholecystostomy. *Convalescence*—normal; in hospital nineteen days. *Postoperative history*—worse than before operation; periodic vomiting; since 1912 has lost her voice; hysteric manifestations.

Gyn. 4110. March 5, 1912. Aged sixty-two years. *Symptoms*—bloody vaginal discharge. *Clinical diagnosis*—myoma uteri; cholelithiasis. *Pathological diagnosis*—adenocarcinoma of fundus; fibro-myoma uteri; gall-stone. *Operation*—hysterectomy; cholecystostomy. *Convalescence*—normal; in hospital thirty-nine days. *Postoperative history*—cured except for sacral backache.

Gyn. No. 4139. March 28, 1912. Aged twenty-six years. *Symptoms*—pain in right iliac fossa; constipation. *Clinical diagnosis*—Lane's kink of ileum; cholelithiasis. *Pathological diagnosis*—obliterative appendicitis; gall-stone. *Operation*—appendectomy; liberation of Lane's kink; cholecystotomy. *Convalescence*—normal; in hospital eighteen days. *Postoperative history*—for six months had intense hyperacidity; no pain in right side; constipation not relieved.

Gyn. No. 4153. April 8, 1912. Aged thirty-five years. *Symptoms*—"abdominal looseness;" weakness in legs; menorrhagia; frequent urination. *Clinical diagnosis*—uterine fibroid; cholelithiasis. *Pathological diagnosis*—fibro-myoma uteri; right hydrohematosalpinx; left hydrosalpinx; obliterative appendicitis; gall-stones. *Operation*—hysterectomy; bilateral salpingo-oöphorectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-eight days. *Postoperative history*—great improvement; pressure symptoms in region of rectum.

Gyn. No. 4207. May 11, 1912. Aged forty-seven years. *Symptoms*—abdominal enlargement; fatigue; abdominal cramps; prolapsus. *Clinical diagnosis*—R. V. O.; uterine fibroid; cholelithiasis. *Pathological diagnosis*—fibro-myoma; gall-stones. *Operation*—plastic; hysterectomy; bilateral salpingo-oöphorectomy; cholecystostomy. *Convalescence*—normal; in hospital twenty-three days. *Postoperative history*—general health markedly improved; complains of surgical menopause.

Gyn. No. 4578. February 5, 1913. Aged forty-three years. *Symptoms*—menorrhagia and metrorrhagia. *Clinical diagnosis*—

myoma uteri; chronic appendicitis; cholelithiasis. *Pathological diagnosis*—fibro-myoma uteri; tuberculosis of uterus and both tubes; peri-appendicitis; gall-stones. *Operation*—plastic; hysterectomy; cholecystostomy; appendectomy. *Convalescence*—prolonged postoperative vomiting; in hospital forty-three days. *Postoperative history*—complete cure.

Gyn. No. 4588³. February 13, 1913. Aged forty-four years. *Symptoms*—vesical irritability and cystocele; menorrhagia; stinging pain in left lower abdomen. *Clinical diagnosis*—R. V. O.; myoma uteri; cholelithiasis. *Pathological diagnosis*—fibromyoma uteri gall-stone. *Operation*—plastic; hysterectomy; cholelithotomy. *Convalescence*—hematoma and superficial infection of gall-bladder wound; in hospital twenty-five days. *Postoperative history*—marked improvement; complains of recurring pain in gall-bladder region; states she was never so well in her life.

A CLINICAL STUDY OF ONE THOUSAND CASES OF CANCER OF THE STOMACH.¹

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IN a study of one thousand cases of gastric cancer it was deemed advisable, so far as it was possible, to compare the character and frequency of the symptoms appearing in this disease with those observed in the cases of gastric ulcer presented to this Association² two years ago.

The 1000 cases of cancer occurred in 10,416 patients affected with various gastric disturbances (9.6 per cent.); this is in comparison to a similar number of cases of peptic ulcer appearing in 12,598 (7.8 per cent.) patients.

The maximum liability to the disease lies between the fortieth and sixtieth year (65 per cent.); the greatest number of cases occurring between the fiftieth and sixtieth years.

AGE. In the following table the number of cases of cancer are presented according to age:

Years.	Cases.	Per cent.
20 to 30	4	0.4
30 to 40	37	3.7
40 to 50	261	26.1
50 to 60	395	39.5
60 to 70	218	21.8
70 to 80	85	8.5

¹ Read at the meeting of the Association of American Physicians, May 12 and 13, 1914.

² AMER. JOUR. MED. SCI., 1912, cliv, 157.

This may be compared with the cases of gastric ulcer in which the largest proportion of cases occurred between the twentieth and fiftieth years as is presented in the accompanying table.

SEX. The greater proportion of cases occur in males; 588 males to 412 females. The following table illustrates the number of cases observed in males and females according to age:

Years.	Cases.	Per cent.
0 to 10	2	0.20
10 to 20	162	16.20
20 to 30	345	34.50
30 to 40	229	22.90
40 to 50	128	12.50
50 to 60	93	9.30
60 to 70	38	3.80
Over 70	3	0.30

Years.	Males.	Females.	Total.
20 to 30	3	1	4
30 to 40	23	14	37
40 to 50	125	136	261
50 to 60	249	146	395
60 to 70	149	75	218
70 to 80	45	40	85
	588	412	1,000

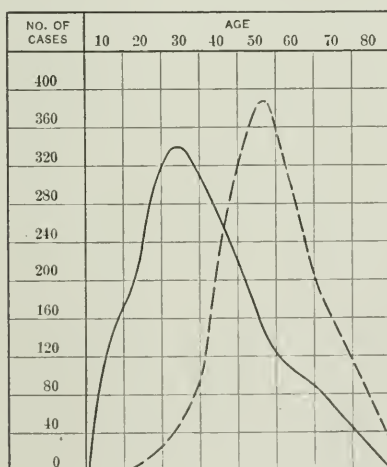


FIG. 1.—Age diagram of one thousand cases of ulcer and one thousand cases of cancer.

This is in comparison with the cases of ulcer in which there were 676 males and 324 females, divided according to age in the following table:

Years.	Males.	Females.	Total.
0 to 10	2	0	2
10 to 20	124	38	162
20 to 30	262	83	345
30 to 40	119	110	229
40 to 50	91	37	128
50 to 60	48	45	93
60 to 70	29	9	38
Over 70	1	2	3

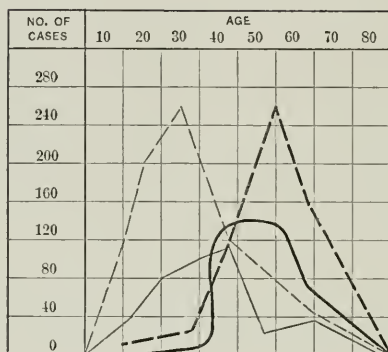


FIG. 2.—Sex and age diagram of one thousand cases of ulcer and one thousand cases of cancer. Dotted heavy black line, male cancer. Solid heavy black line, female cancer. Dotted light black line, male ulcer. Solid light black line, female ulcer.

NATIONALITY. The following table indicates the relative proportion of cases among various nationalities, 75 per cent. being Americans:

Nationality.	Number.	Per cent.
American	753	75.3
German	123	12.3
Russian	96	9.6
English and Irish	17	1.7
South American	5	0.5
Other countries	6	0.6

RACE. Of the 1000 cases there were 948 whites and 52 colored, that is, 94.8 per cent. whites and 5.2 per cent. colored.

The small proportion of colored persons noted is due to the fact that but a small number of colored patients come under our observations. The following table indicates the number of colored males and females classified according to age:

Age.	Males.		Females.		Total	
	Cases.	Per cent.	Cases.	Per cent.	Cases.	Per cent.
30 to 40	2	3.4	0		2	3.4
40 to 50	2	13.4	3	5.7	10	19.2
50 to 60	16	30.7	9	17.3	25	47.0
60 to 70	9	17.3	3	5.7	12	23.0
70 to 80	3	5.7	0		3	5.7
	37	70.5	15	28.7	52	

There were 37 males (70 per cent.) to 15 females (28 per cent.), the largest number occurring between the fiftieth and sixtieth years.

HEREDITY. An hereditary history of cancer appearing in various portions of the body occurred in 104 of the 1000 cases (9.4 per cent.). Of these there were:

	Cases.
With a family history of cancer of the stomach	22
" " " " " " uterus	37
" " " " " " breast	24
" " " " " " throat	5
" " " " " " rectum	11
" " " " " " face	5
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The following table indicates the ages of the cases presenting a family history of cancer showing that the largest proportion of cases occur in those years in which the greatest number of cases of cancer of the stomach occur:

Age.	Cases.	Cases with family history of cancer.
20 to 30	4	0
30 to 40	37	0
40 to 50	261	33
50 to 60	395	44
60 to 70	218	22
70 to 80	85	5
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TRAUMA. A definite history of trauma was elicited in 19 cases, in 6 of which there had been blows on the abdomen.

ANEMIA. In 229 of our cases in which hemoglobin estimations had been recorded, anemia was present in 189 (82 per cent.). The average of the hemaglobin estimations was 43.

CARDIAC AND VASCULAR CHANGES. Chronic endocarditis was present in 114 cases (11.4 per cent.); arteriosclerosis in 696 (69.6 per cent.) of all cases.

As is observed in the following table the largest proportion of cases of cancer with arteriosclerosis occurred after the fiftieth year of life.

Age.	Cases.	Cases with arteriosclerosis.	Per cent. of cases with arteriosclerosis.
20 to 30	4	0	.0
30 to 40	37	0	.0
40 to 50	261	89	12.7
50 to 60	396	321	46.1
60 to 70	218	201	28.7
70 to 80	85	85	12.5

BLOOD-PRESSURE. Of the 132 cases in which blood-pressure examinations were recorded, 121 (91 per cent.) present readings

of 170 mm. or more. The following table presents this condition at various ages:

Age.	Cases with blood-pressure 170 to 180 mm.	Cases with blood-pressure, 180 to 190 mm.	Cases with blood-pressure 190 to 200 mm.	Cases with blood-pressure 200 to 210 mm.	Total.
40 to 50	2	5	4	1	12
50 to 60	21	12	13	8	54
60 to 70	7	22	6	3	38
70 to 80	1	7	4	5	17
Total	31	46	27	17	121

Renal Changes. Records of urinary examinations were recorded in 717 of the 1000 cases; albumin was present in 401 (55.9 per cent.), and albumin and casts in 334 (46.4 per cent.).

PREVIOUS DISORDERS OF DIGESTION. In the 1000 cases of cancer there was a history of some previous digestive trouble in 232 cases (23.2 per cent.). Of the 232 cases, 109 had slight attacks of indigestion for a period of five years or more preceding the present gastric disease, while 25 had slight attacks only during the last five years preceding the present disease. Of the remaining 123 cases, 32 had chronic indigestion more or less all their lives, of which 29 had chronic indigestion, mainly during the last five years preceding the present illness. Seventy-three cases gave a definite history of former gastric ulcer. It is therefore evident that of these 1000 cases, but 23 per cent. presented a history of any previous digestive disturbance whatever, even in the slightest degree, and that but 7.3 per cent. give a direct history of ulcer. If, therefore, all of the former digestive disturbances be considered as due to ulcer the formation of gastric cancer from ulcer could not have taken place in more than 23 per cent.; if all of these cases with slight digestive disturbances be disregarded in our series, this percentage is reduced even to 12.3 per cent.

EXCESSES IN FOOD AND DRINK. A history of former indiscretions in diet was obtained in 321 instances (32.1 per cent.), and in but 137 (13.7 per cent.) did the patient attribute his disease to some specific error in diet. A history of alcoholism was obtained in 152 instances (15.2 per cent.).

INFECTIOUS DISEASES. A history of syphilis was obtained in 79 instances; tuberculosis of the lungs was present in 48 instances.

THE GASTRIC SECRETION IN CANCER. Of the 1000 cases the gastric secretion was examined in 733 instances:

	Cases.	Per cent.
Normal acidity was observed in	23	3.1
Hyperchlorhydria was observed in	35	4.1
Hypochlorhydria was observed in	21	2.8
Anacidity was observed in	654	89.2

Over 89 per cent. of our cases presented an entire absence of free hydrochloric acid. In comparison with the 810 cases of ulcer in which the gastric secretion was examined the result is as follows:

	Cases.	Ulcer. Per cent.	Cases.	Cancer. Per cent.
Normal acidity was observed in	376	46.4	23	3.1
Hyperchlorhydria was observed in	246	30.3	35	4.9
Hypochlorhydria and acidity in	188	23.2	675	92.0

Of the 733 cases, consisting of 443 males and 290 females, the acidities are as follows:

	Males.	Per cent.	Females.	Per cent.
Normal acidity	16	2.1	7	0.9
Hyperchlorhydria	17	2.3	18	2.5
Hypochlorhydria	13	1.7	8	1.1
Anacidity	397	54.1	257	35.2

LACTIC ACID. Lactic acid was present in 601 instances, or 81.9 per cent. of the 733 cases in which the gastric secretion was examined. It was present only in any appreciable amount in those cases in which there was a complete absence of free hydrochloric acid.

OPPLER-BOAS BACILLI. The Oppler-Boas bacilli were observed in 582 cases, or 79.3 per cent. of the 733 cases. They were found only in those instances in which lactic acid was observed.

Sarcina were observed in 24 instances (32 per cent.).

Visible blood was observed in the gastric contents in 129 instances (7.5 per cent.).

Coffee-ground contents was obtained in 653 instances (61.8 per cent.).

Röntgen-ray examinations were made in 32 instances, 8 cases presenting cancer at the cardiac region and 24 at the pyloric region. In those instances with cancer at the cardia a dilatation of the esophagus was revealed. In 5 of these cases the condition was confirmed by means of the esophagoscope. In the Röntgen-ray examination of the pyloric cases the characteristic sawed-off pylorus with retention was observed and frequently a filling defect.

SYMPTOMS. *Onset.* Of the 1000 cases, 232 (23.2 per cent.) presented histories of some previous digestive disturbance, while 759 (75.9 per cent.) gave histories of sudden acute onset; attributing the origin of the disorder to some definite error in diet in 137 cases (13.7 per cent.). In the remaining 9 (0.9 per cent.) the character of the onset could not be determined. From the following table it is evident that proportionately the largest number of younger patients affected with cancer are found among those individuals who have had previous digestive disturbances; the reverse is true of those cases in which the disease comes on acutely without previous digestive upsets:

Years.	No.	MALES.			No.	FEMALES.		
		Acute onset.	Previous digestive trouble.	Undetermined.		Acute onset.	Previous digestive trouble.	Undetermined.
20 to 30	3	2	1	0	1	0	1	0
30 to 40	23	3	19	1	14	5	9	0
40 to 50	125	77	46	2	136	99	35	2
50 to 60	249	47	32	0	146	102	44	0
60 to 70	143	112	29	2	75	65	9	1
70 to 80	45	42	3	0	40	35	4	1
Total	588	453	130	5	412	306	102	4

Of the 73 cases that gave a distinct evidence of former gastric ulcer the largest proportion occurred in younger individuals, that is before the fiftieth year of life; the large number occurred in males. The following table illustrates this condition:

Years.	Total cases.	MALES.		Total cases.	FEMALES.	
		Evidence of former gastric ulcer			Evidence of former gastric ulcer.	
		No.	Per cent.		No.	Per cent.
20 to 30	3	0	.0	0	0	.0
30 to 40	23	12	16.4	14	6	8.2
40 to 50	125	19	26.0	136	15	20.5
50 to 60	249	11	15.0	146	6	8.2
60 to 70	143	3	4.1	75	1	1.3
70 to 80	45	0	.0	40	0	.0
	588	45	61.5	412	28	38.2

DURATION OF LIFE. The duration of life in cancer of the stomach varies greatly. In 472 of the 1000 cases (278 males and 194 females) by far the greatest number of deaths occurred between six and twelve months after symptoms were first observed both in males and females and the smallest number between twelve and eighteen months.

Years.	Total number of cases in which duration of symptoms were noted.																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																												
	Total males.		Cases with duration of life up to 3 months.					Cases with duration of life from 3 to 6 months.					Cases with duration of life from 6 to 12 months.			Cases with duration of life from 12 to 18 months.		Cases with duration of life from 18 to 24 months.		Cases with duration of life over 2 years.																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																									
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The above table illustrates this condition. From it is evident that of the 472 cases in which the duration of life was noted 316 cases (182 males and 134 females) died within one year of the first appearance of symptoms of the disease, 104 (59 males and 45 females) died between one and two years and 52 (37 males and 15 females) died after two years.

ACUTE CASES. Of the 472 cases of the 1000 cases, 88 (53 males and 35 females), or 18.6 per cent., ran an acute course, that is, these patients died within three months after the appearance of the first symptoms.

LONG DURATION. *Chronic Course.* Of the 472 (37 males and 15 females), 11 per cent. ran a chronic course, that is, a course of over two years.

PERIODS OF IMPROVEMENT IN WEIGHT AND GENERAL CONDITIONS. Of the total number (472) in which duration of symptoms were noted, during almost the entire course of the disease, 145 (30.8 per cent.), 93 males and 52 females) presented periods of improvement in weight and general conditions.

GAIN IN WEIGHT AND GENERAL IMPROVEMENT WITH AMELIORATION OF SYMPTOMS. Of the 145 cases presenting periods of improvement (93 males and 52 females) 26 males showed a gain in weight from five to thirty-five pounds, while the remaining 67 showed improvement in the general condition, with amelioration of symptoms; 11 females showed a gain in weight from five to twenty pounds while the remaining 41 showed improvement in the general condition with amelioration of symptoms. The following table illustrates this condition:

Years.	MALES.						
	Cases with periods of improvement.	Gain of five pounds.	Gain of ten pounds.	Gain of fifteen pounds.	Gain of twenty pounds.	Gain of thirty pounds.	Gain of thirty-five pounds.
20 to 30	0	0	0	0	0	0	0
30 to 40	3	1	1	0	0	0	0
40 to 50	11	1	3	0	2	0	0
50 to 60	33	2	2	3	0	1	0
60 to 70	35	1	1	3	2	0	1
70 to 80	11	0	1	1	0	0	0
Total	93	5	8	7	4	1	1

FEMALES.						
20 to 30	0	0	0	0	0	
30 to 40	1	0	0	1	0	
40 to 50	18	1	1	2	1	
50 to 60	23	1	0	2	1	
60 to 70	6	0	0	0	0	
70 to 80	4	1	0	0	0	
Total	52	3	1	5	2	

PERIODS IN MONTHS OF GAIN IN WEIGHT AND GENERAL IMPROVEMENT WITH AMELIORATION OF SYMPTOMS. Of the 145 cases presenting periods of improvement with amelioration of symptoms

and gain in weight the improvement occurred in the greatest number of cases for one or two months (that is, in 79 per cent. of all cases) after the beginning of treatment; after this period the number of cases presenting improvement are less and less.

MALES.

Years.	Cases without periods of improvement.	One month.	Two months.	Three months.	Four months.	Five months.	Six months.	Seven months.
20 to 30	0	0	0	0	0	0	0	0
30 to 40	3	1	0	2	0	0	0	0
40 to 50	11	3	4	2	1	1	0	0
50 to 60	33	8	13	6	5	1	0	0
60 to 70	35	9	24	2	0	0	1	1
70 to 80	11	5	5	0	1	0	0	0
Total	93	26	44	12	7	2	1	1
Per cent.		17.9	30.3	8.2	4.7	1.4	0.7	0.7

FEMALES.

Years.	Cases with periods of improvement.	One month.	Two months.	Three months.	Four months.	Five months.	Six months.	Seven months.	Eight months.
30 to 40	1	0	1						
40 to 50	18	14	2	0	0	0	0	0	0
50 to 60	23	10	8	2	1	1	0	0	0
60 to 70	6	4	2	0	0	1	0	1	1
70 to 80	4	3	0	0	1	0	0	0	0
Total	52	31	13	2	2	2	0	1	1
Per cent.		2.3	9.5	1.4	1.4	1.4	0	0.7	0.7

LATENT CANCER. There were 12 cases (1.2 per cent.) in which the disease was unsuspected or in which the symptoms due to the associated disease were so marked and the gastric symptoms so slight or absent that the disease was unsuspected or only detected shortly before death. The cases in this class are arranged in the following table according to age and sex and according to the suspected disease.

MALES.

Years.	No. of cases.	Unsuspected.	Chronic nephritis.	Arterio-sclerosis.	Anemia.	Cardiac disease.	Tuberculosis.
40 to 50	1	0	0	0	0	0	1
50 to 60	2	0	0	0	1	1	0
60 to 70	3	1	1	1	0	0	0
70 to 80	2	0	1	1	0	0	0
Total	8	1	2	2	1	1	1

FEMALES.

Years.	No. of cases.	Chronic nephritis.	Arterio-sclerosis.	Anemia.	Cardiac disease.
40 to 50	1	0	0	0	1
50 to 60	1	1	0	0	0
60 to 70	2	0	1	1	0
70 to 80	0	0	0	0	0
Total	4	1	1	1	1

DYSPHAGIA. Dysphagia existed in 69 instances, namely, in those cases in which the growth involved the cardiac orifice, that

is, in 6.9 per cent. of all cases. Of the 69 cases, 60 per cent. represented males and 40 per cent. females. The following table includes the number of cases presenting this condition among males and females arranged according to age:

Years.	Males.	Per cent.	Females.	Per cent.
20 to 30	0	.0	0	.0
30 to 40	2	2.8	0	.0
40 to 50	4	5.6	6	8.6
50 to 60	17	24.6	10	14.5
60 to 70	11	15.9	7	10.2
70 to 80	18	11.2	4	5.6
Total	42	60.1	27	38.9

LOSS OF WEIGHT. Of the 1000 cases the weight on admission was noted in 839 instances. Of this number 743 (98.5 per cent.) presented a loss of weight of from five to seventy-eight pounds.

PAIN. Of the 1000 cases pain was present in 931 (93.1 per cent.)

Effect of Food on Pain. Of the 931 cases with pain the symptoms appeared immediately after taking of food in 191 cases (20.5 per cent.); several hours after meals in 83 instances (9.9 per cent.), and in 616 instances (66.1 per cent.) it was not influenced by food, while in 41 cases 4.4 per cent. it appeared irregularly, at times bearing some relation to the ingestion of food and at other times not. This condition is to be contrasted with our cases of ulcer in which there were 940 cases with pain; this symptom appeared within the first hour after meals in 223 instances between one and two hours in 188, after two hours in 491, and in 38 it appeared irregularly.

Relation of Pain to Acidity. Of the 733 cases in which gastric secretion was examined pain appeared in 672 (91.5 per cent.)

	Cases.	Absent.		Moderate.		Moderately severe.		Severe.	
		No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Normal acidity	23	2	0.2	1	0.1	8	1.1	12	1.7
Hyperchlorhydria	35	3	0.4	5	0.7	10	1.4	18	2.6
Hypochlorhydria	21	4	0.5	3	0.4	5	0.7	11	1.6
Anacidity	654	52	7.0	112	16.6	136	20.2	351	52.2
	733								

The relation of pain to acidity is presented in the table above, from which it is evident that pain is more pronounced in those instances associated with a low acidity. The reverse is true in cases of ulcer in which pain is most pronounced in those cases associated with high acidity, as is observed in the following table:

	Cases.	Absent.		Moderate.		Moderately severe.		Severe.	
		No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Normal acidity	376	2	0.2	92	11.3	123	15.1	159	19.6
Hyperchlorhydria	246	1	0.1	8	9.0	35	4.3	202	24.9
Hypochlorhydria	188	7	0.7	59	7.3	82	10.1	40	5.0
	810								

Location of Pain. In 561 instances of all of the 931 cases affected with pain the pain extended more or less over the whole abdomen;

it was limited to the epigastric region in 229 instances; in 68 to the lower abdomen; in 62 to the back, and in 11 to the chest.

TENDERNESS. Of the 1000 cases, tenderness was present in 893 cases (89.3 per cent.). The tenderness was localized in special areas in 265 cases (26.5 per cent.), and was general over the entire abdomen in 628 (62.8 per cent.). This condition is to be contrasted with that found in ulcer in which of the 1000 cases epigastric tenderness was present in 908 cases (90.8 per cent.). A tender area was noted to the right of the median line in 41 cases (4.1 per cent.); a dorsal, together with an epigastric, tender spot in 523 instances (52.3 per cent.); a dorsal area alone in 25 (2.5 per cent.).

ANOREXIA. Anorexia was present in 893 of our 1000 cases, or 89.3 per cent. The symptoms varied markedly from a slight loss of appetite to an absolute aversion for food. The 893 cases are divided into 516 males and 377 females. The following table illustrates the degree of anorexia among males and females according to age:

Years.	MALES.					FEMALES.				
	Slight. No. Per cent.	Moderate. No. Per cent.	Intense. No. Per cent.	Variable. No. Per cent.		Slight. No. Per cent.	Moderate. No. Per cent.	Intense. No. Per cent.	Variable. No. Per cent.	
20 to 30	1 0.1	0 0	1 0.1	0 0.0		0 0	0 0	0 0	0 0	
30 to 40	4 0.4	6 0.6	7 0.7	2 0.4		2 0.2	5 0.5	3 0.3	2 0.2	
40 to 50	36 4.0	25 2.8	31 3.4	4 0.4		41 4.5	20 2.2	59 6.6	13 1.4	
50 to 60	51 5.7	89 9.9	76 8.6	18 2.0		31 3.4	51 5.7	44 4.9	7 0.7	
60 to 70	21 2.3	56 6.2	45 5.6	12 1.3		11 1.2	16 1.6	34 3.8	5 0.5	
70 to 80	9 1.0	4 0.4	16 1.8	2 0.2		6 0.6	8 0.8	17 1.9	2 0.2	
Total	122	180	176	38		91	100	157	29	

EFFECT OF FOOD ON VOMITING. Vomiting is a prominent symptom, occurring in 893 (89.3 per cent.). This symptom appeared immediately after the ingestion of food in 182 (20.3 per cent.); several hours after meals in 74 (8.2 per cent.), while in 599 cases (67 per cent.) it was not influenced by food, and in 38 (4.2 per cent.) it appeared irregularly, seeming at times to bear some relation to the ingestion of food and at times not.

Vomiting and Pain. Of the 931 cases with pain vomiting occurred in 862 instances (92.6 per cent.). Of the 931 cases in which pain appeared there were 191 having pain immediately after meals, of which 158 had vomiting. There were 83 with pain several hours after meals, of which 76 had vomiting. There were 616 not influenced by the ingestion of food, of which 593 had vomiting, and in 41 instances the pain appeared irregularly, of which 35 had vomiting.

The following table illustrates this condition:

Time of appearance.	Cases with pain.		Cases with vomiting and pain.		Per cent. of cases of vomiting in comparison with cases with pain.
	No.	Per cent.	No.	Per cent.	
Immediately after meals	191	20.5	158	18.3	82.7
Several hours after meals	83	8.9	76	8.8	91.5
Not influenced by meals	616	66.1	593	68.7	96.2
Appearing irregularly	41	4.4	35	4.0	85.3
Total	931		862		

In the 69 cases of cancer not accompanied by pain, vomiting occurred in 31 cases (45 per cent.). In our cases of ulcer the vomiting was proportionately more frequently observed in those instances in which pain appeared early, as is observed in the following table:

Time of appearance of pain.	Cases with pain	Cases with vomiting	Percentage of cases of vomiting in proportion to the cases with pain.
In one hour	223	194	87.0
In one to two hours	188	143	76.6
After two hours or irregularly	529	324	61.2
	<hr/> 940	<hr/> 661	

RELATION OF VOMITING TO ACIDITY. Of the 733 cases in which the gastric secretion was examined, vomiting appeared in 655 (89.3 per cent.). The relation of vomiting to acidity is illustrated in the accompanying table, from which it is apparent that by far the largest proportion of cases with severe vomiting are associated with anacidity.

	Total cases.		Absent.		Moderate.		Severe.	
	No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Normal acidity	25	1	.01		8	1.2	14	2.1
Hyperchlorhydria	35	4	.05		12	1.8	19	2.5
Hypochlorhydria	21	3	.04		7	1.0	11	1.6
Anacidity	654	70	9.50		191	29.1	393	60.0
	<hr/> 733	<hr/> 78			<hr/> 218		<hr/> 437	

These cases are to be contrasted with the ulcer cases in which vomiting is definitely more prominent in those instances accompanied by high acidity.

Acidity.	Cases.	Moderate vomiting.		Severe vomiting.	
		No.	Per cent.	No.	Per cent.
Normal acidity	298	125	23.5	171	32.5
Hyperchlorhydria	138	18	3.3	122	22.8
Hypochlorhydria	95	76	14.3	19	3.5

HEMATEMESIS. Gastric hemorrhage occurred in 227 cases (25.4 per cent. of those patients in which vomiting was present, and in 22.7 per cent. of the whole number. The following table presents the cases with gastric hemorrhage arranged according to age and sex:

	Males.		Females.	
	No.	Per cent.	No.	Per cent.
30 to 40	2	0.8	1	0.4
40 to 50	41	18.0	14	6.1
50 to 60	94	41.4	18	7.9
60 to 70	49	21.5	3	1.3
70 to 80	3	1.3	2	0.8
	<hr/> 189	<hr/> 83.0	<hr/> 38	<hr/> 16.5
Total				

The following table presents the proportion of cases according to age, accompanied by a single hemorrhage, and those by multiple

hemorrhages; 88.7 per cent. of these cases presented multiple hemorrhages and but 10.8 per cent. single hemorrhages.

Years.	Cases.	Per cent. of cases with hemorrhages.	Proportion of cases with single hemorrhages.		Proportion of cases with multiple hemorrhages.	
			No.	Per cent.	No.	Per cent.
30 to 40 . . .	3	1.2	0	0	3	1.3
40 to 50 . . .	55	24.1	5	2.0	50	22.0
50 to 60 . . .	112	49.3	11	4.8	101	44.4
60 to 70 . . .	52	22.8	8	3.4	44	19.3
70 to 80 . . .	5	2.1	1	0.4	4	1.7
Total . . .	227	99.5	25	10.8	202	88.7

To be contrasted with these cases are the cases of ulcer in which a much larger proportion of cases were accompanied by single hemorrhages (38.7 per cent.) and but 60 per cent. with multiple hemorrhages. Of the 227 cases with hematemesis the hemorrhages were small in 151 cases, profuse in 62, and variable in 14. The blood was coffee-ground or dark in 202, bright red in 18, and variable in 7.

MELENA. Tar-colored stools or a history of this condition was present in 189 of the 1000 cases, that is, in 18.9 per cent. In the following table is illustrated the number and percentage of these cases at various ages, the largest proportion appearing between the fiftieth and sixtieth years:

Years.	Cases with melena.	Percentage of cases with melena.
30 to 40	1	0.1
40 to 50	46	4.6
50 to 60	97	9.7
60 to 70	43	4.3
70 to 80	2	0.2
Total	189	18.9

These cases are to be contrasted with the same condition occurring in ulcer in which tar-colored stools occur much more frequently, that is, in 51.5 per cent., the largest proportion appearing between the tenth and thirtieth years. Noting the proportion of cases with melena in comparison with those with hematemesis it is evident, as is illustrated in the following table, that gastric hemorrhage is much more frequent than melena:

COMPARISON OF CASES WITH HEMATEMESIS AND MELENA AT VARIOUS AGES.

Years.	Gastric hemorrhage.		Melena.	
	Cases.	Per cent.	Cases.	Per cent.
30 to 40	3	0.3	1	0.1
40 to 50	55	5.5	46	4.6
50 to 60	115	11.2	97	9.7
60 to 70	52	5.2	43	4.3
70 to 80	5	0.5	2	0.2
Total	227		189	

If these cases be contrasted with those of ulcer it is evident that in ulcer the reverse condition exists, that is, melena is over twice as frequent as gastric hemorrhage.

OCCULT BLOOD. The test for occult blood in the stools was rarely omitted. The feces were examined in 642 of the 1000 cases. Of these a positive reaction was obtained in 594 (92.5 per cent.). The examination only included those cases in which visible blood was absent or had not appeared for some time before the test had been made. When once occult blood was observed in these cases it could usually again be found at any time afterward; this is not true of ulcer, for in this latter condition the blood is not always present in the first test, but frequently appears sometime during the course of the disease. In the ulcer cases positive tests for occult blood were obtained in 86.6 per cent.

OCCULT BLOOD AS AN EARLY SIGN OF CANCER. Of the 642 cases in which tests for occult blood were made in the feces, 216 were early cases. Of these 201 (93 per cent.) presented occult blood, indicating that the presence of occult blood is a very constant as well as early sign of gastric cancer.

TUMORS. Of the 1000 cases a mass (tumor) was detected in 719 (71.9 per cent.) some time during the course of the disease. Arranged according to age and sex these cases may be divided as follows:

Years.		No.	Males.	No.	Females.
			Per cent.		Per cent.
20 to 30	.	1	0.1	0	0
30 to 40	.	11	1.1	10	1
40 to 50	.	98	9.8	103	10.3
50 to 60	.	175	17.5	133	13.5
60 to 70	.	108	10.8	47	4.7
70 to 80	.	20	2.0	13	1.3
Total		413		306	

Of the 719 cases in which a mass could be palpated 217 presented this condition within six months after the first appearance of symptoms, that is, 30.1 per cent., while in 502 it was presented after six months (69.9 per cent.), from which it is evident that the appearance of a palpable tumor is over twice as common after the first six months after the first appearance of symptoms than before this period.

Location of Growth. From a clinical point of view cancer of the stomach may be divided into those located at the cardia, those at the pylorus, and those involving the stomach generally. Of the 1000 cases the involvement is as follows:

	No.	Per cent.
Pyloric area	589	59.9
Cardiac area	69	6.9
General involvement	306	30.6
Undetermined	36	3.6
Total	1000	

Divided among males and females and according to age the involvement may be tabulated as follows:

Years.	No.	MALES.				No.	FEMALES.			
		Pyloric.	Cardia.	General involvment.	Undetermined.		Pyloric.	Cardia.	General involvment.	Undetermined.
20 to 30	0	0	0	1	2	1	0	0	0	1
30 to 40	23	17	2	2	2	14	8	0	6	0
40 to 50	125	75	4	41	5	136	67	6	61	2
50 to 60	249	157	17	87	8	146	80	10	54	2
60 to 70	143	92	11	34	6	75	36	7	28	4
70 to 80	345	33	8	2	2	40	24	4	10	11
Total	588	374	42	147	25	412	215	27	159	11

SECONDARY CANCER OF THE STOMACH. Of these there were 9 (0.9 per cent.) in our series; 3 were secondary to breast cancer; 2 were secondary to rectal cancer; 4 were secondary to uterine cancer. The remainder, 991 (99.1 per cent.), were primary cancers.

DILATATION OF THE STOMACH. Dilatation of the stomach was present in 467 instances. Arranged according to age and sex this condition is presented in the following table, indicating that the largest percentage of cases occur in males between the fiftieth and seventieth years of life:

Years.	No.	Males.		No.	Females.	
		Per cent.			Per cent.	
20 to 30	0	0.0		0	0.0	
30 to 40	3	0.6		1	0.2	
40 to 50	52	11.1		61	13.0	
50 to 60	147	31.2		72	15.4	
60 to 70	89	19.0		31	6.6	
70 to 80	5	1.4		6	1.1	
Total	296	62.9		171	36.3	

Peristaltic movements were observed in 411 cases.

Perforation occurred in 23 cases (2.3 per cent.) of our series. Arranged according to age and sex these cases may be classified as follows:

Years.	No.	Males.		No.	Females.	
		Per cent.			Per cent.	
30 to 40	1	4.3		0	0	
40 to 50	5	21.7		2	8.6	
50 to 60	4	17.3		3	13.0	
60 to 70	5	21.7		1	4.3	
70 to 80	2	8.6		0	0	
Total	17	73.6		6	25.9	

FEVER. Of the total number of cases, 472 in all, in which the symptoms were noted almost during the entire course of the disease, fever occurred in 203 cases (43 per cent.). Of these 73 ran a temperature of between 99° and 100°, 66 between 100° and 101°, and 45 between 101° and 102°.

Temperature.	No. of cases.	Per cent. of cases.
99° to 100°	73	15.4
100° to 101°	66	13.7
101° to 102°	45	9.5
102° to 103°	13	2.7
103° to 104°	6	1.2
With temperature	203	43.0
Without temperature	269	57.0

Of the 203 cases in which fever was present 37 (18.2 per cent.) had fever during the entire course of the disease; 52 (25.6 per cent.) developed fever during the first six months of the disease, while 151 (74.3 per cent.) first developed fever after the sixth month of the disease. Fever is only present therefore in about 18 per cent. of cases during the entire course of the disease; but 25 per cent. of cases develop fever during the first six months of the disease, and 74 per cent. of the cases develop fever after six months, indicating that fever is a late manifestation of the disease.

ASCITES AND EDEMA OF THE EXTREMITIES. Ascites or edema appeared in 211 (21.1 per cent.) of our cases. Ascites appeared alone without edema in 44 cases (4.4 per cent.); edema appeared without ascites in 104 cases (10.4 per cent.); edema and ascites appeared together in 63 cases (6.3 per cent.). Of the 211 cases with ascites or edema but 53 (24.6 per cent.) presented these signs before the first six months after the first appearance of symptoms, while 158 (74.7 per cent.) presented these signs after the first six months, indicating that both ascites and edema are late manifestations in gastric cancer.

JAUNDICE. Jaundice was presented in 32 of our cases (3.2 per cent.). It was present as a late manifestation of the disease, in every instance appearing only after the symptoms of the disease had been present for over six months.

Metastases. Metastases were noted in 672 (67.2 per cent.) of our cases; of these:

255 (37.9 per cent.) occurred in the glands.
222 (33.0 per cent.) occurred in the liver.
54 (8.0 per cent.) occurred in the peritoneum.
45 (6.6 per cent.) occurred in the pancreas.
41 (6.1 per cent.) occurred in the intestines.
14 (2.0 per cent.) occurred in the lung.
12 (1.7 per cent.) occurred in the spine.
2 (0.3 per cent.) occurred in the skin.
27 (4.0 per cent.) undetermined.

It is evident that over 70 per cent. of the metastases appeared in the glands and in the liver.

BOWEL MOVEMENTS. The bowels moved normally in 67 cases (6.7 per cent.); diarrhea existed in 249 cases (24.9 per cent.); constipation existed in 572 cases (57.2 per cent.). The bowels were variable, that is, constipation alternating with diarrhea in 112 cases (11.2 per cent.).

MENTAL CONDITION. Of the 1000 cases depression of more or less severe type was noted in 861 instances (86.1 per cent.). Of this number actual melancholia was observed in 9 instances (0.9 per cent.). The depression is usually noted early in the disease, but becomes more severe as the disease progresses.

OPERATIONS. Of the entire number operation was performed in 265 instances (26.6 per cent.). Of this number 138 (51.8 per cent.) were exploratory laparotomies. Gastro-enterostomies were performed in 98 (36.9 per cent.); gastrostomies in 21 (7.8 per cent.), and pylorectomies and gastrectomies in 9 (3.3 per cent.).

DURATION OF LIFE FOLLOWING EXPLORATORY LAPAROTOMY. In the 126 of the 138 cases we were able to follow the cases sufficiently to determine the duration of life following the exploratory incision. It is evident that death ensues within a year in most instances, and but few cases are observed surviving over a year.

Years.	MALES.						FEMALES.					
	For 3 months after operation.	From 3 to 6 months.	From 6 to 12 months.	From 12 to 18 months.	From 18 to 24 months.	From over 2 years.	For 3 months after operation.	From 3 to 6 months.	From 6 to 12 months.	From 12 to 18 months.	From 18 to 24 months.	For over 2 years.
30 to 40	1	1	0	0	0	0	2	0	0	0	0	0
40 to 50	2	2	0	0	2	0	3	6	6	0	1	1
50 to 60	8	14	4	0	2	1	12	9	3	0	1	0
60 to 70	8	7	7	4	1	0	6	0	2	1	0	0
70 to 80	3	2	0	1	0	1	5	0	1	0	0	0
Total	22	26	11	5	5	2	18	15	18	1	2	1

DURATION OF LIFE FOLLOWING GASTRO-ENTEROSTOMIES. In 7 of the 98 cases the patients could not be followed, and the duration of life of these cases could not be determined. As is evident from the following table the largest proportion of cases die within one year following this operation, though a few survived as much as two years and over:

Years.	MALES.						FEMALES.					
	For 3 months after operation.	From 3 to 6 months.	From 6 to 12 months.	From 12 to 18 months.	From 18 to 24 months.	For over 2 years.	For 3 months after operation.	From 3 to 6 months.	From 6 to 12 months.	From 12 to 18 months.	From 18 to 24 months.	For over 2 years.
30 to 40	2	0	0	0	1	0	1	0	0	0	0	0
40 to 50	5	4	5	0	2	1	1	2	2	0	6	3
50 to 60	3	2	6	0	3	3	1	2	2	1	4	0
60 to 70	6	1	7	1	2	1	1	0	1	1	2	0
70 to 80	1	2	0	2	0	0	2	0	1	0	0	0
Total	17	9	18	3	8	5	6	4	6	2	10	3

DURATION OF LIFE FOLLOWING GASTROSTOMY. As is indicated in the following table, most of the cases die within a year after the operation of gastrostomy.

Years.	MALES.						FEMALES.					
	For 3 months.	From 3 to 6 months.	From 6 to 12 months.	From 12 to 18 months.	From 18 to 24 months.	For over 2 years.	For 3 months.	From 3 to 6 months.	From 6 to 12 months.	From 12 to 18 months.	From 18 to 24 months.	For over 2 years.
30 to 40	0	0	0	0	0	0	1	0	0	0	0	0
40 to 50	0	2	0	0	0	0	1	0	1	0	0	0
50 to 60	3	3	1	0	1	0	0	1	0	1	0	0
60 to 70	1	0	1	1	0	0	1	0	1	0	0	0
70 to 80	0	1	0	0	0	0	0	0	0	0	0	0
Total	4	6	2	1	1	0	3	1	2	1	0	0

DURATION OF LIFE FOLLOWING PYLORECTOMIES AND GASTRECTOMIES. Of the 9 cases operated on, but one lived for eighteen months after operation.

Years.	MALES.						FEMALES.					
	For 3 months after operation.	From 3 to 6 months.	From 6 to 12 months.	From 12 to 18 months.	From 18 to 24 months.	For over 2 years.	For 3 months.	From 3 to 6 months.	From 6 to 12 months.	From 12 to 18 months.	From 18 to 24 months.	For over 2 years.
30 to 40	0	0	0	0	0	0	0	0	0	0	0	0
40 to 50	0	1	0	1	0	0	0	1	1	0	0	0
50 to 60	0	1	1	0	0	0	0	2	0	0	0	0
60 to 70	0	0	0	0	0	0	1	0	0	0	0	0
70 to 80	0	0	0	0	0	0	0	0	0	0	0	0
Total	0	2	1	1	0	0	1	3	1	0	0	0

POSITION OF GROWTH AS DETERMINED AT OPERATION OR AUTOPSY. The number of cases observed were 284. Of these the location of the growth is as follows.

	No.	Per cent.
In the pyloric area	166	58.4
In the cardiac area	19	6.6
In the lesser curvature	23	8.1
In the greater curvature	12	4.2
In the fundus	8	2.8
General involvement	56	19.7

CONCLUSIONS. From a careful study of the 1000 cases of cancer of the stomach the following conclusions may be drawn:

1. Of patients suffering with various gastric disturbances, 9.6 per cent. are affected with cancer while but 7.8 have ulcers.

2. The largest proportion of cancers occur between the fortieth and sixtieth years of age, while the largest proportion of ulcers occur between the twentieth and fiftieth years.

3. The greatest number of cases occur in males (588 males and 412 females).

4. Of patients affected with gastric cancer there is an hereditary history of cancer in 9.4 per cent.

5. A definite history of trauma occurs in 1.9 per cent. of cases.

6. Anemia is present in 82 per cent.; chronic endocarditis in 11 per cent.; arteriosclerosis in 69 per cent.

7. Seven per cent. give a direct history of former ulcer, and only in 23 per cent. could the cancer have formed from ulcer.

8. A history of overindulgence in food or drink can be obtained in about half the number of cases of cancer.

9. The greatest proportion of cases of cancer present an acidity, that is, 89 per cent.; 3 per cent. show a normal acidity; 4 per cent. an hyperacidity, and 3 per cent. a subacidity. Lactic acid is present in 81 per cent.; the Oppler-Boas bacilli in 79 per cent.; sarcinae in 32 per cent.; coffee-ground contents in 61 per cent.

10. The average duration of life is less than one year in 66 per cent. of all cases, between one and two years in 22 per cent., and over two years in 11 per cent.

11. Periods of improvement, including gain in weight, are not uncommonly observed for a short time in cancer of the stomach.

12. Latent cancer occurs in 1 per cent. of the cases.

13. Dysphagia is present in 7 per cent. of the cases and pain the most frequent of all symptoms in 93 per cent. Tender abdominal areas are present in 69 per cent.

14. Anorexia and vomiting are most prominent symptoms, being present in 89 per cent. of cases.

15. Hematemesis is present in 25 per cent. of all cases and melena in 19 per cent. Occult blood appears in the stools in 92.5 per cent.

16. The tumor was sufficiently advanced to be palpable in 72 per cent. of cases, but only in 30 per cent. of these cases within a half year of the first appearance of symptoms, while in 60 per cent. of cases this symptom was manifested after the first six months.

17. Clinically in 60 per cent. of cases the cancer is located at the pyloric area, in 7 per cent. at the cardiac area, and in 30 per cent. there is a general involvement.

18. Ninety-nine per cent. of the gastric cancers are primary and but 1 per cent. represent secondary growths.

19. Dilatation of the stomach occurs in 47 per cent. of cases.

20. Perforation occurs in 2 per cent., and fever in 43 per cent.; ascites and edema in 21 per cent.; jaundice in 3 per cent., and metastases are present in 67 per cent.

21. Operation was performed in 28 per cent. of cases; in 52 per cent. of these there were exploratory laparotomies; in 37 per cent. gastro-enterostomies; in 8 per cent. gastrostomies, and in 3 per cent. pylorectomies and gastrectomies. In but a small proportion of cases did the patients survive over a year after operation.

22. As determined by operation or autopsy the location of the growth was as follows: in 59 per cent. there was pyloric involvement; in 8 per cent. cardiac involvement; in 8 per cent. involvement of the lesser curvature; in 4 per cent. of the greater curvature; in 2 per cent. of the fundus, and in 19 per cent. there was a general involvement.

The early diagnosis of cancer of the stomach is usually quite difficult, for the most important symptoms may be absent even though the growth may have already assumed considerable proportions.

The most important sign of this disease, the presence of a palpable tumor, is observed in 72 per cent. of cases, and yet in 60 per cent. of cases it makes its appearance six months after the first appearance of symptoms, and it cannot therefore be relied upon as an early sign of the disease.

The absence of free hydrochloric acid is a frequent sign, as it is present in 89 per cent. of cases, and yet the condition is so frequent in other conditions that it loses much of its value.

Signs of pyloric obstruction with consequent dilatation are noted at times, and when present early are of the greatest diagnostic importance. According to my experience one of the most constant signs as an early manifestation of the disease is the presence of occult blood in the stools. It was present in 92.5 per cent. of our cases. The continued occurrence of this sign whenever there is a suspicion of cancer points rather certainly to the presence of this disease.

A history of some previous digestive trouble was observed in 232 cases (23 per cent.). Of these 109 had slight attacks of indigestion for a period of five years or more preceding the present gastric disease, while 25 had slight attacks during the last five years preceding the present disease. Of the remaining 123 cases, 23 had chronic indigestion more or less all of their lives, of which 29 had chronic indigestion mainly during the last years preceding the present illness.

Seventy-three cases gave a definite history of former gastric ulcer. It is therefore evident that in the 1000 cases but 23 per cent. presented a history of any previous digestive disturbance whatever even in the slightest degree, and that but 7.3 per cent. gave a direct history of ulcer. If therefore all of the former digestive disturbances be considered as due to ulcer the formation of gastric cancer from ulcer could not have taken place in more than 23 per cent.; if all of the cases with slight digestive disturbances

be disregarded in our series this percentage is reduced even to 12.3 per cent. I therefore believe that from a study of my own cases from a clinical point of view, as well as from the pathological studies of Aschoff, that the figures of Wilson and MacCarty (71 per cent.), so often referred to, are far too high, and that while I am convinced that gastric ulcers are at times transformed into malignant growths, I do not believe that this change takes place in more than 23 per cent. of cases, and possibly is not even so large a proportion.

Of the entire number of my cases, operations were performed in 266 instances (26.6 per cent.). Of these 138 (51.8 per cent.) were exploratory operations. Gastro-enterostomies were performed in 98 (36.9 per cent.); gastrostomies in 25 (7.8 per cent.), and pylorectomies and gastrectomies in 9 (3.3 per cent.). Of these there is not one patient living. It is therefore evident that the early diagnosis of cancer of the stomach is still fraught with difficulty, and that until more certain methods are available exploratory incisions should be urged upon all persons over forty years of age having gastric symptoms, which are not relieved after a few weeks' treatment, especially is this the case if there be some loss of flesh, an absence of free hydrochloric acid in the gastric contents, and occult blood in the stools. Even under these conditions many cases will be operated on too late, for there can be no question but that gastric cancer may be present for some time and may assume considerable proportions even before marked symptoms of indigestion are manifested. Inasmuch as in a certain proportion of cases gastric ulcers become cancerous, it is well in all operations for gastric ulcers to consider the advisability of performing excision or partial gastrectomy to prevent any possibility of the transition of ulcer into cancer.

SOME CLINICAL ASPECTS OF GASTRIC HEMORRHAGE.¹

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In November, 1906, I had a patient, a woman, aged thirty-eight years, in whose case I had made a diagnosis of acute gastric ulcer. This patient, about sixteen months previously, had been operated on, while under my care, for supposed gall-stones. At the operation no gall-stones were found, but a dense adhesion held the fundus of the gall-bladder to the lower pole of a movable right kidney. The

¹ Read before the American Gastro-enterological Association, annual meeting held at Atlantic City, June 22, 1914.

gall-bladder was drained. The stomach was carefully examined for ulcer, but evidence of such a lesion could not be found. When at the above-mentioned date the diagnosis of gastric ulcer was made it was with some misgivings, even though all of the cardinal symptoms excepting hemorrhage were present. At that time routine tests for occult blood were not being made, neither had the Einhorn silk-string test yet been suggested. However the hunger pains at a definite time, the hyperchlorhydria, the nausea and vomiting, and the localized tenderness were so definitely and obstinately present that I at once withheld all food by mouth and instituted rectal feeding. After three days of rectal feeding the patient had a slight hemorrhage from the stomach. This was November 10, 1906. On the following day she had a frank and profuse hemorrhage, and blood was found in large amount in the stool. The usual treatment for gastric hemorrhage was undertaken. At the end of a week of unsuccessful effort a surgeon was called in consultation and a posterior gastro-enterostomy was advised on account of the continuance of hemorrhages after one week of unsuccessful medical treatment. At the operation the base of a large ulcer was found on the gastric side of the pyloric ring. After the operation the hemorrhage ceased and the patient made a slow but satisfactory recovery. This was the first and only operation for hemorrhage I have had done in over 500 patients having gastric or duodenal ulcer and in over 150 patients having gastric carcinoma.

The striking feature of the case was the sudden, profuse, and obstinate hemorrhage from the stomach soon after discontinuing food by mouth. The patient had been upon a modified rest treatment with rather forced feeding, as it was supposed, on account of certain marked nervous symptoms, and from the fact that the stomach had been seen and handled just fifteen months previously and no ulcer was found, that it was a case of simple hyperchlorhydria.

In the past ten years, or since the experience narrated, I have seen at least six cases of gastric or duodenal ulcer when sudden marked and alarming hemorrhages occurred immediately upon withholding food by the mouth. I have also noticed this in a few cases of gastric carcinoma. One of the gastric ulcer cases, of which I shall speak later, proved fatal. This was the only fatal hemorrhage in 500 cases of gastric or duodenal ulcer. It has occurred to me in the past few years that there is a definite sequence of events which may well be considered in the relation of cause and effect when a frank hematemesis or melena occurs, after the sudden withholding of food in the treatment of ulcer. It is the purpose in this paper, therefore, to refer more particularly to the clinical aspects of hemorrhage due to benign or malignant ulceration in the stomach or duodenum and to venture a few conclusions as to diagnosis and treatment. Hemorrhage from causes other than ulceration will not be considered now.

The frequency of hemorrhage in gastric or duodenal ulcer must necessarily be an open question. Statistics differ widely. The extremes are 21 per cent., reported by Lebert, and 81 per cent. reported by Joslyn. It is gratifying to see that among the members of this association there is a greater unanimity. Stockton estimates about 33 per cent., and Friedenwald reports in 1000 cases, hematemesis 22.8 per cent. and melena 51.5 per cent.

Upon due consideration one can easily see that the frequency of hemorrhage in ulcer is a question which does not lend itself to unquestioned statistical information. It would be almost inconceivable that an ulcer in any portion of the gastro-intestinal canal could pass through the various pathological stages without contaminating to a greater or less degree the stomach contents or the feces with blood at some time or other. Boas has long been emphasizing this point, and in an article in the *Deutsche medizinische Wochenschrift*, May 28, 1914, again calls our attention to it. It would be better to report that blood has been observed by the physician in charge in so many cases, and that blood has been reported to have been seen by the patient or nurse in so many cases. Even then the statistics cannot be of much value, for the reports from patients are frequently unreliable, and even those of physicians and nurses may not always be depended upon. Unless a chemical or microscopic test is made, one can easily be deceived by naked-eye appearances. In my own cases blood was either seen or reported to have been seen or found chemically in about 43 per cent. I am quite sure it was evident at some time or other in the remaining 57 per cent., but was not observed or detected. The 43 per cent. includes all patients who have had blood in the gastric contents or stool, either seen by the physician or patient or a competent observer, or detected by tests for occult blood or by the Einhorn string. Various tabulations show rather interesting results. Of 440 patients, 316 were gastric and only 114 duodenal. The reason for the comparatively small number of duodenal ulcers is that we insisted upon rather more definite information before making a diagnosis of duodenal ulcer. When an ulcer was suspected, but could not be definitely located, it was called gastric. Of the gastric ulcer 104 were males and 212 females. Of the duodenal 71 were males and only 43 females. Melena was observed about three times more frequently in duodenal than in gastric ulcer. Of 87 patients having the string test, 43 were positive. A physician in general practice who recognizes but few cases of gastric ulcer because he seldom makes the diagnosis without the presence of microscopic blood may report a much higher percentage of hemorrhages than one in special or consultation practice. There is no doubt that many cases of gastric or duodenal ulcer are recognized by the consultant and specialist and treated as such only after the acute condition has subsided. The symptoms which the patient presents, therefore, are

due to the damage resulting from the previous acute ulceration. This damage, as is well known, may be of the nature of extensive scar tissue, of adhesions, and of chronic localized peritonitis, as well as of altered gastric and intestinal secretion and motility and also of certain well-marked neuroses. It is very evident unless the initial lesion, that is the acute ulceration, is definitely recognized and differentiated from the end-results of the ulceration, much well-meant treatment will be misdirected and of no benefit to the patient.

	Gastric ulcer.	Per cent.	Gastric cancer.	Per cent.	Duodenal ulcer.	Per cent.
Number of cases, 588	332		135		121	
Male	109	33	93	69	75	62
Female	223	67	42	31	46	38
Evidence of blood—	147	44	61	45	49	40
Male	57	52	41	44	26	35
Female	90	40	20	48	23	50
History of—						
Hematemesis	60	...	15	...	11	
Melena	23	...	8	...	11	
Observed—						
Hematemesis	24	...	15	...	6	
Melena	1	...	1	...	0	
Test meal, blood—						
Positive	66	57	32	61	20	35
Negative	49	43	20	39	37	65
String stain—						
Positive	42	68	9	75	21	55
Negative	20	32	3	25	17	45
Stool, occult blood—						
Positive	18	56	12	57	7	37
Negative	14	44	9	43	12	63

The Einhorn string test is a helpful aid in determining the presence of an acute ulcer or an acute exacerbation of a chronic ulcer. It appears that the negative findings of a string are more reliable than the positive. A positive string is only an evidence that blood has stained the string. This blood may have come from any break in the continuity of the mucous membranes, minute or extensive. To conclude that an ulcer is present when a string is positive is unwarranted. I have seen this demonstrated in the operating room a number of times. On the other hand a negative string test does not prove that an old or even a recently healed ulcer with all the consequent damage is not present. I have seen a number of cases operated for ulcer which had presented a negative string, and yet a large granulated, apparently healed ulcer was found in the excised pylorus. The test for occult blood in the stomach contents or in the feces is also a valuable aid, but it is even more difficult to interpret than the Einhorn string test. Unless one examines the mouth carefully, uses the proctoscope routinely, and supervises the diet definitely it is absolutely impossible to make a correct interpretation of the finding of occult blood. For some time past I have attempted to differentiate between a benign ulcer of the stomach and duodenum and ulceration due to malignancy by certain definite vari-

ations in the string test and in the test for occult blood. It seemed to me that a blood-stain which extended along the string some distance, say two, three, or four inches, in an irregular degree of intensity, frequently mingling with the bile stain, was very likely to be the evidence of malignancy, while a very definite stain, of say, a half-inch of string, with an otherwise clean or unstained string, was very likely to be the evidence of a simple benign ulcer. I also thought the continuous finding, day after day, of occult blood in the stool or the stomach contents was a rather definite evidence pointing to malignancy. But in the operating room and from the reports from the pathological department I have been completely disillusionized and therefore no longer attempt to differentiate with these tests.

Leaving these rather fragmentary remarks on the frequency and significance of the presence of blood in ulceration I return to the original theme, namely, the relation of a frank hemorrhage to the sudden withholding of food from the stomach. I am sure from the number of times I have noticed this in the care of patients having ulcer or carcinoma that it is more than a mere coincidence. I therefore think it needs interpretation and that a proper interpretation may be of assistance in determining the safe course of treatment of these cases.

My interpretation of this phenomenon must unfortunately be based in part on theory. The cause of ulceration of the stomach is not known. The theory most accepted is probably lowered general vitality, localized traumatism, and increased or changed secretions as the chain of events which leads to the formation and continuation of an ulcer. All other theories advanced, whether that of arteriosclerosis, of embolism, or of infection, seem to depend upon the presence of one or more of these three conditions to insure the development of a true peptic ulcer. Hydrochloric acid is an irritant to all tissues except the normal mucous membrane of the stomach. When the mucous membrane of the stomach suffers an injury, hydrochloric acid immediately becomes an irritant even there. Albuminous foods combine with hydrochloric acid and prevent the corrosive action upon an ulcer. Other foods, such as fats, seem to protect the ulcer from the acid. It would seem reasonable, therefore, to conclude that the sudden withholding of certain foods from the ulcerated stomach would increase the irritating action of hydrochloric acid and further the ulceration; and this I think will explain the occurrence of the frank hemorrhages in the cases to which I refer. If this is a correct inference our methods of treatment of gastric and duodenal ulcer in the acute stage should be changed accordingly. In January, 1904, Lenhartz reported a treatment which has since gone by his name. It has since then occasionally been referred to enthusiastically. The principles upon which this treatment was based were these:

1. It permitted the opportunity of furnishing highly nourishing food of almost sufficient caloric value at a time when the body was below par and specially needed to be brought up to a higher efficiency.

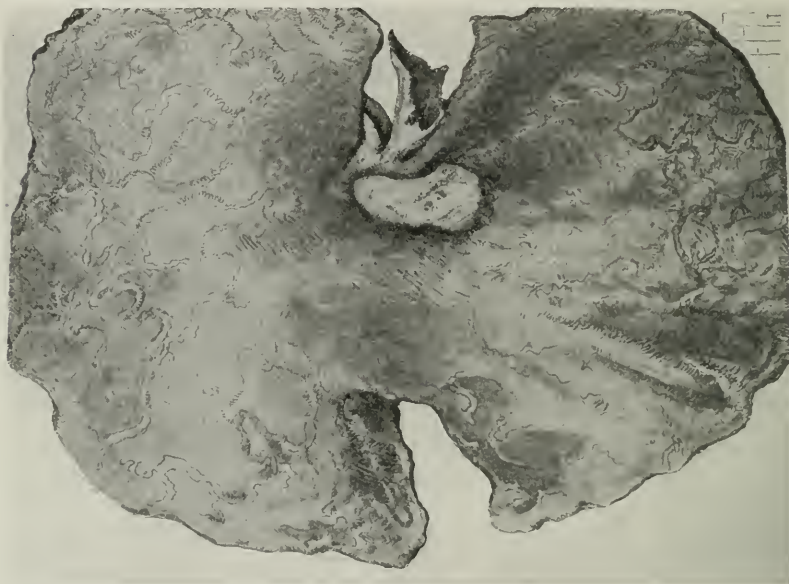
2. On account of the small amount of food given at each feeding it prevented distention of the stomach.

3. It prevented the action of the excessive hydrochloric acid upon the raw ulcerating surface by combining it with a food albumin.

This treatment never appealed to me as worthy of general application, because it has always seemed that the short period of five or eight days of rest to the stomach, which is usually all the time necessary to start healthy granulation, could produce very little harm so far as lowered vitality is concerned. On the other hand the advantage of prompt healing with as little damage to the tissues as possible is so great that one would hesitate to abandon the time-honored principle of complete rest of the part affected. However, since my results with the cases referred to were so disastrous I am experiencing a change of view so far as the third principle of the Lenhartz treatment is concerned. This change of view is not so much because of the better or more prompt final results but because of the possibility of avoiding dangerous hemorrhage and possible perforation. I report a case which will illustrate this point:

In May, 1912, I saw a patient, aged forty-three years, who gave a definite history of chronic gastric ulcer. He had had a frank gastric hemorrhage three months previously. When I first saw him he had slight pains in the epigastrium, some pyrosis, felt weak and nervous, and was sleepless. He was thin and emaciated. He had dieted closely and starved himself. A gastric analysis showed free HCl 72, combined 10, and total 92; no blood or mucus. The string test was negative. It was concluded that the ulcer was healed and that his anxiety over the return of a hemorrhage produced most of his symptoms. He was placed upon a diet, suitable to his condition, of a high caloric value, and also given alkalies, nitrate of silver, and bromides. In a short time he gained twenty pounds in weight and was up to his usually efficiency. For two years he did an enormous amount of work in founding and organizing a research department in a university. In January, 1914, he returned with his former symptoms. At this time the gastric analysis revealed the same condition as before, a hyperchlorhydria, but he had a definitely positive string test. It was concluded he had a return of ulcer of the stomach. Food was immediately withheld from the mouth, bismuth subcarbonate in large doses was administered, and glucose solution, 56 gm. to the liter, was given per rectum. Within two days he had severe epigastric pain, followed with a profuse hemorrhage from the stomach and with the appearance of blood in the stool. He also gradually developed the symptoms of marked acidosis. These hemorrhages continued from time to time regardless of treatment, and in eighteen days the patient died. At the autopsy

a large indurated ulcer was found in the lesser curvature near the pylorus. The omentum was adherent opposite the base of the ulcer and two distinct vessels plugged with a small thrombus, three-eighths inch apart, were plainly visible. This can be seen in the accompanying sketch.



Indurated ulcer in the lesser curvature near the pylorus.

The pyloric ring was contracted with the scar of an old ulcer. Both ulcers were benign as reported by the pathological department of the Mercy Hospital. The futility of any treatment but immediate surgical interference was plainly evident. This was not done at once because of the profound shock and acidosis, and could not be done subsequently because of the repeated profuse hemorrhages. This was the first and only patient of the series upon which these clinical observations are based who died from hemorrhage due to benign ulcer. A number of consultations were held with my medical and surgical colleagues of Pittsburgh as well as with men from distant cities. The questions always arose, Shall this patient continue with complete rest of the organ affected or shall he have feeding by mouth? or shall the abdomen be opened and the stomach and duodenum explored? The last question was invariably and emphatically answered negatively by the surgeons. The other two, resting or feeding, were not so harmoniously agreed upon by the sulting internists. This brings to our consideration the treatment

for hemorrhage due to benign ulceration. In a paper by Deaver¹ the following assertion is made referring to gastric erosion: "My belief in the necessity of the operation in this class of cases has been considerably undermined by the good results of medical treatment." Referring to acute peptic ulcer, "If appropriate measures are taken the hemorrhage is rarely dangerous and seldom repeated." Of chronic benign ulcer, "There are groups of cases to which operation for hemorrhage should be confined." This comes with all the greater emphasis as it is the conclusion of a man who is skilful with the knife and one whose papers usually bristle with statements attempting to show the culpability of the internist for "keeping" undoubted surgical patients under medical treatment. When surgical interference is excluded what shall be the measures adapted to meet so alarming and apparently grave condition? While I am thoroughly convinced that it is a mistake suddenly to withhold all food by the mouth in the treatment of ulcer, especially when there is a decided hyperchlorhydria, it seems to me when a frank hemorrhage is evident all food should be discontinued at once and for two to four days. The alkaline blood of itself protects the ulcer as well or better than food can, and a stomach without food will have less peristalsis than one with food. The formation of a thrombus sufficient to plug a bleeding vessel requires as nearly absolute rest as possible. This is a surgical principle which cannot be violated by any procedure based upon doubtful physiological and chemical theories. Absolute rest is essential: it must be rest of body, of mind, and as nearly as possible rest of the stomach. Opiates will be necessary, an ice-bag on the epigastrium, and by the Murphy method, glucose solution should be given per rectum. If this is impossible it should be given subcutaneously. If the diagnosis of a chronic ulcer has been made and the hemorrhage has been of the severe type, surgical interference should be seriously considered after the patient has recovered from the shock of the first hemorrhage.

The following conclusions might be offered upon the fragmentary experiences recorded:

1. The statistics of hemorrhage from the stomach whether of hematemesis or melena, or as revealed by occult blood-tests, or by string tests, are of very little value.

2. In the treatment of acute peptic ulcer, or acute exacerbation of chronic ulcer, especially when accompanied with hyperchlorhydria, food should not be held from the stomach at once.

3. Surgical treatment for gastric hemorrhage has a very limited but definite field.

¹ Surgery, Gynecology, and Obstetrics, March, 1914.

LABORATORY DIAGNOSIS IN THE EARLY STAGES OF CONGENITAL SYPHILIS.

BY CLIFFORD G. GRULEE, A.M., M.D.,

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IN some recent work which I have been doing it has occurred to me that many cases of latent congenital syphilis have been overlooked. This has occurred, it has seemed, because of the general tendency of most physicians to regard a positive or negative Wassermann as of far greater importance than any physical findings. Those most familiar with the Wassermann reaction are least likely to take this exaggerated view of its usefulness. The above statements probably apply more to the first few weeks of life than to any other period. It seems to me to be of use, therefore, to examine carefully into the various laboratory methods which may be used to further our knowledge before the appearance of such active symptoms as will make all such tests unnecessary.

It should be said in starting that either clinicians have gone very far astray in their judgment of what constitutes congenital syphilis in this period or else the laboratory tests are to a certain extent very misleading. Rietschel¹ says: "These children before the outbreak of an exanthem neither clinically, serologically, nor cytologically show the slightest sign of a lues." By most French clinicians the presence of an enlarged spleen is regarded as most suggestive of luetic taint at this period, and when this is combined with a history of syphilis in the parents and the presence of epitrochlear glands one may feel a strong suspicion at least that a luetic condition exists.

The following body fluids are frequently examined with an idea to ascertaining the nature of a disturbance in the early weeks of life:

Urine.

Blood.

Cerebrospinal fluid.

URINE. There is very little of diagnostic value to be found in the urine of a luetic infant. While it is true that in many of these cases at autopsy a chronic inflammatory condition of the kidney is to be found, still, as a rule, this does not show clinically. At best the clinical findings in a case of nephritis at this age would be confusing, especially in the first days of life when albuminuria from other cause is comparatively frequent.

BLOOD. Routine examination of the blood shows conditions that vary markedly in the first few weeks of life, and especially the first

¹ Med. Klinik, 1909, v, 658.

few days. This should make us skeptical about interpreting findings at this time which would seem to point to syphilis. Lymphocytosis, or rather the predominance of mononuclear lymphocytes, is a normal finding at this age, and the variation of 5 per cent. or even 10 one way or the other is of sufficient frequency in cases other than syphilitic to be of little value from a diagnostic stand-point. The number of leukocytes is so variable that any decrease or increase within the limits which would be expected in congenital syphilis makes comparatively little difference in differentiating the condition.

We come now to the question of the value of the Wassermann reaction in these cases. It seems to be a well-established fact that in over 90 per cent. of clinically certain cases of congenital syphilis the Wassermann reaction is positive. This, however, tells us little. We know so little about the true reason for the appearance of the Wassermann reaction that the interpretation of such a finding is not as evident as it may appear. One would think that if all cases of congenital syphilis positive clinically give a positive Wassermann reaction, that then all cases of congenital syphilis should do the same; and while this may be true to a greater or less extent, still the occurrence of a florid syphilis probably means the presence in the blood of those bodies which are most likely to produce a positive Wassermann. The absence of such bodies from the blood, so far as our present knowledge goes, does not by any means exclude the presence of an active syphilis. The findings of Rietschel² and of Ledermann³ prove the usefulness of the Wassermann in cases of congenital syphilis. They do not account for such conditions, however, as are recorded by Halberstädter, E. Müller, and Reiche⁴ in scarlet fever where temporarily at least a positive Wassermann reaction was obtained in five of ten cases, nor in another of their cases where syphilis developed after a negative Wassermann had been obtained. Nor do they account for such cases as those of Cassoute,⁵ who obtained different reactions in twins, nor of Niemann,⁶ who gives the account of a peculiar form of disease as yet not classified in which the Wassermann reaction was distinctly positive. We may say from this, therefore, that while in the active stages of the disease a positive Wassermann is of distinct value, the negative is of comparatively little, since many cases of syphilis unquestionably exist in which the blood gives no positive Wassermann reaction. But even a positive Wassermann reaction may go astray, as in the case reported by Niemann. It would be well now to look into the condition of affairs as they exist in the newborn infant and in the first few weeks of life. Most German authorities have satisfied themselves with the statement that sufficient data is not present to

² Loc. cit.

³ Arch. f. Derm. u. Syph., 1911, cvi, 325.

⁴ Berl. klin. Woch., 1908, xlv, 1917.

⁵ Bull. de la Soc. de Péd. de Paris, 1913, xv, 179.

⁶ Jahrb. f. Kinderheilk, 1914, lxxix, 1.

draw any positive conclusions as to the value of the Wassermann reaction at this stage. The subject, however, has been exhaustively treated by Bar and Daunay.⁷ The examination carried on by these investigators was made on the blood from the umbilicus⁸ of fifty-seven newborn infants, the blood being tested immediately after birth. These cases were divided into four groups:

Group 1. Fourteen born of mothers with florid syphilis.

Group 2. Eleven born of mothers with syphilitic symptoms, not of a florid type.

Group 3. Fourteen born of mothers with suspected syphilis.

Group 4. Eighteen born of mothers well or apparently well.

Bar and Daunay distinguish four reactions: (1) The strongly positive, (2) the partially positive, (3) doubtful, and (4) negative. In Group 1:2, or 14.28 per cent., were positive; 1, or 7.14 per cent., partial; 6, or 42.84 per cent., doubtful, and 5, or 35.71 per cent., negative. In Group 2:2, or 22.22 per cent., were positive, while 7, or 78.78 per cent., were negative. In Group 3:4, or 28.51 per cent., were positive; 1, or 17.04 per cent., partial, 2, or 14.28 per cent., doubtful, and 7, or 50 per cent., negative. Of the children in Group 4, 6 were examined immediately after birth. Of these, 1, or 16.66 per cent., gave partial reaction, 1, or 16.66 per cent., doubtful, and 4, or 66.66 per cent., negative. Of 12 children that were examined somewhat later 2, or 16.66 per cent., gave positive Wassermann; 1, or 18.08 per cent., partial; 4, or 33.33 per cent., doubtful, and 5, or 41.66 per cent., negative. From these statistics they draw the following conclusions:

1. The method of Wassermann does not necessarily give concordant results in the mother and her infant.

2. Of 34 cases there has been agreement only 16 times, or 46.53 per cent.

3. The agreement is less where the maternal syphilis is florid (4 times in 14 cases, or 38.57 per cent.) than in the cases where the maternal syphilis is old or non-florid, 12 times in 20 cases, or 60 per cent.

4. In the majority of cases where there has been agreement the result has been negative in both mother and infant.

5. When there has been disagreement it is shown to be more often positive in the mother (9 in 18 cases).

Further, there is an analysis of 13 infants born of mothers with syphilis or a condition which was at least strongly suspicious and who gave negative reactions. Of these 1 showed no signs of syphilis later; 9 presented unquestioned syphilitic lesions; and of the 3 who died, 1 was distinctly syphilitic, and 1 a monster. Bar and Daunay state that the positive result in the newborn has the same significance as that in the mother, but that the significance of par-

⁷ *L'Obstétrique*, 1909, ii, 1, 192, 260.

⁸ Exceptions are noted below.

tial or doubtful reactions is greater in the newborn probably because of biliary pigments in the blood.

CEREBROSPINAL FLUID. The routine examination of cerebrospinal fluid at this period brings some interesting but not conclusive evidence. The globulin content as estimated by the Nonné or Noguchi tests while giving positive reaction in a certain proportion of cases certainly does not do this in all, even in the active stages, so that while the evidence of a positive reaction is suggestive it is by no means conclusive, and even when present may signify the presence of other conditions than congenital syphilis. The cell content is practically always increased, though this too is subject to wide variation, so much so that Baron⁹ concludes that no dependence can be put upon the number of the cells present nor upon the differential count. There is a widespread opinion that in syphilis in general the number of cells is increased and the large proportion of these cells are mononuclear in type. While this holds good to a large extent in congenital syphilis, still the finding is not so general as to be of much value in differentiating the condition.

Recently, Lange has suggested a test by the use of a colloidal gold chloride solution in different dilutions of cerebrospinal fluid. This test was based on the fact that certain albuminous bodies when brought in contact with a solution of colloidal gold in the presence of an electrolyte would, in certain concentration, cause a clumping together of the smaller colloidal particles, producing various changes in color and even precipitation. This test was originally devised for the purpose of distinguishing *tabes dorsalis* and *paretic dementia*. By some it is held that this test represents merely a means of determining the presence of albuminous bodies in the cerebrospinal fluid, and hence is of little more value than are such tests as the Nonné and Noguchi. The theory on which the test is based is certainly contrary to this opinion, since the colloidal gold clumps at different dilutions with different albumin bodies, though at present it is not possible to state positively at just what dilutions certain albumin bodies produce this reaction. It seems to me that one can be readily convinced of a certain degree of specificity in this reaction if he will note the regularity with which the cerebrospinal fluids from certain conditions produce reaction in certain dilutions. With the idea of testing this reaction in congenital syphilis, Dr. Moody and myself¹⁰ tested the cerebrospinal fluid of 9 cases of typical congenital syphilis, in every case of which reaction was strongest in the dilution of 1 to 40 and 1 to 80. In one case which was tested within six weeks and found positive, the reaction at thirteen weeks after seven weeks of treatment was negative. In many of these cases the Nonné test looked quite doubtful and the Wassermann on the cerebrospinal fluid was very frequently negative. In 7 cases of

⁹ *Jahrb. f. Kinderheilk.*, 1909, lxi, 25.

¹⁰ *Jour. Amer. Med. Assoc.*, 1913, lxi, 13.

suspected congenital syphilis in all but one the same reaction held true. In one the reaction was the same as the one obtained in parietic dementia, the child died a few days after the removal of the fluid. Unfortunately no autopsy was obtained. In one the reaction was very weak and the subsequent course led one to think that the case if syphilitic at all had only a slight taint. Of these 14 cases only 3 came within the time mentioned as the doubtful period, but of these all 3 showed distinct positive reactions, and the course of the disease subsequently was altogether confirmatory of the presence of congenital syphilis. Of non-syphilitic cases there seems to be one type which is likely to give a reaction in the same dilution as does that of congenital syphilis. This is the meningismus or serous meningitis. In the two cases in our series affected with pneumonia complicated by meningismus or serous meningitis both gave the greatest reaction in dilutions of 1 to 40 and 1 to 80. In one of these, syphilis could not be absolutely ruled out. In the other one there was certainly no clinical evidence of the condition, and subsequent tests led us to think that this was a source of error. While the data at hand is too small to allow conclusions of a positive nature to be drawn, still the findings as brought out in this series of cases is distinctly suggestive, and it is possible that in the Lange test we have a means of confirming any suspicions which we may have of syphilis in the early months of life. The test is a very easy one to perform and may be carried out without much special equipment, provided the solution of colloidal gold chloride is prepared in a laboratory. While at first it was thought very difficult to prepare this, a little experience seems to have overcome these difficulties.

The consideration of this subject would not be complete without taking into account the recently proposed luetin test of Noguchi.¹¹ With this test the writer has had very little experience, and hence must depend almost altogether upon the reports of Noguchi. Of these, for our purpose, comparatively few are useable. Of Holt's 33 cases 15 were between the ages of one and three months. Of these 12 were positive and 3 negative. All positive cases had been given mercurial treatment previous to the reaction, while the 3 negative cases had received no such treatment, 73 non-syphilitic cases gave negative reaction. The Noguchi luetin reaction, therefore, is in much the same state as is the gold chloride reaction. Both need much confirmatory evidence in order to affirm or deny their importance.

CONCLUSIONS. 1. There is no test which is proved to be pathognomonic of congenital syphilis in the early stages between the birth and the development of active symptoms.

2. The examination of the urine and the routine examination of cerebrospinal fluid for globulin content and cells offers little evidence of value for the diagnosis of this stage of the disease.

¹¹ Serum Diagnosis of Syphilis, Philadelphia, 1912, 179.

3. The evidence as to the Wassermann reaction all goes to show the unreliability of the test at this age.

4. The Lange gold chloride reaction on the cerebrospinal fluid offers at present some hope that the evidence obtained in this way may be of distinct benefit.

5. So far as we may judge from the luetin test as at present reported active treatment with mercury materially influences it, so much so that without the mercurial treatments no cases have as yet proved positive. It may be said, however, that the Noguchi test has a distinctly negative value, inasmuch as in all cases not syphilitic the reaction was negative.

MODERN METHODS OF TREATMENT OF SYPHILIS OF THE NERVOUS SYSTEM.

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THE discoveries of Schaudinn, Wassermann, Ehrlich, and Noguchi have led to great changes in the methods of diagnosis and of treatment of syphilitic disease of the central nervous system. Those of us who have enjoyed the privilege of testing these newer methods on a large number of hospital and private patients have also the duty of reporting the results obtained and the conclusions reached.

Omitting from present consideration all our earlier cases, we have the records of about 120 cases to form the basis of this study. It is no easy matter to arrive at just conclusions in a subject so full of pitfalls. The spontaneous remission and exacerbations of all syphilitic forms of central nervous disease make it particularly difficult to ascertain accurately the effect of any form of treatment. Hence the necessity of observing an impartial, critical attitude toward the newer remedies and methods applied to the treatment of these conditions.

We have included in the list of cases 55 cases of tabes, 20 of general paresis, 41 of cerebral and cerebrospinal lues, 3 of optic neuritis, and 2 of specific spondylitis.

PRESENT METHODS. Every patient admitted to our service in the hospital, especially if syphilitic disease of the nervous system is suspected, is subjected to a lumbar puncture for routine examination of the spinal fluid. A Wassermann test is made, using the fluid in quantities up to 1 c.c., according to the method of Hauptmann and Hoessli, and the cell count is estimated as soon as possible after the withdrawal of the spinal fluid. The Fuchs-Rosenthal

chamber is used for this purpose. The globulin content is determined by the butyric acid method of Noguchi. In each case a Wassermann test of the patient's blood is also made.

We desire to sound a warning against indiscriminate lumbar puncture. After all the procedure is not indifferent or agreeable, and in every case the patient should be kept on his back for at least eighteen hours after the puncture. Intense headache and symptoms of meningeal irritation are apt to follow the operation, more especially if this precaution is not observed. We anesthetize the site of the puncture by infiltration of the region between the spinous processes with 0.5 per cent. novococain solution. In cases treated by a series of intraspinal injections the fluid is withdrawn for examination at the time of administering the serum, thus obviating the necessity of puncturing the patient merely to determine the influence of treatment.

SEROLOGICAL TECHNIQUE. In the performance of the Wassermann test we have adhered to the original technique with the following variations: (1) For the sake of economy we have reduced the total quantity by half, using 0.1 c.c. of serum as the maximum quantity instead of 0.2 c.c., as in the original test, and have reduced all the other ingredients proportionately. (2) We use as antigen the extract of normal beef or guinea-pig heart, extracted in alcohol, and fractionated by the addition of acetone according to the method of Noguchi. The acetone insoluble fraction is taken up in pure methyl alcohol and titrated for both anticomplementary (auto-inhibitory) and hemolytic properties as well as to determine its property to bind complement in the presence of syphilitic serum. We have used none but those extracts which have proved as sensitive as the alcoholic extract reinforced with cholesterin, but which showed much less tendency to hold up hemolysis in the presence of normal serum. A double quantity of the antigen extract was always used as a control and never showed any inhibitory action. The complement was titrated each time before doing the tests, care being taken to avoid an excess of complement in view of the fact that a large number of human sera contain an excess of normal antishoop amboceptor, which, in addition to the two units added in the test, is responsible for the failure to detect cases of syphilis giving only partial fixation.

We have never observed any tendency of the spinal fluid to act in an anticomplementary manner, and for this reason have not hesitated to use as much as 1 c.c. (0.5 c.c. in our system) of the fluid for the test.

All our tests are incubated for one-half hour in a water-bath at 37° C., and then are placed in the ice-box for about two or three hours before adding sheep cells. A further refinement is introduced at this point. Instead of adding two units of amboceptor with the cells or of adding sensitized sheep cells, the cell suspension alone is

added and the tests placed again in the water-bath for ten minutes. At the end of this time it will be easy to note those sera that contain normal antish sheep amboceptor in sufficient quantity to lase completely the control tube. To these no further hemolysin is added, while to all the other tests the usual double hemolytic dose is added. It is in this way that the presence of natural or normal sheep amboceptor is detected and the addition of an excess of hemolysin resulting often in completely lasing a weakly inhibited serum is avoided.

The tests after completion were placed in the ice-box or left at cool-room temperature and the readings were taken within an hour and usually again the next morning.

TREATMENT. We have been guided in our treatment of the clinical condition by the outcome of the various biological reactions. If the examination has shown the presence of an active luetic process, intensive treatment was administered. Under such conditions it has been our routine practice to give a series of salvarsan injections intravenously at intervals of seven to ten days, the average dose being 0.25 gram to 0.4 gram. After four to six injections of salvarsan have been given the patients receive a series of intramuscular injections of salicylate of mercury in 0.5 to 1 grain doses. These injections are given weekly until from ten to fifteen injections have been administered. We have given several courses of treatment as outlined above, discharging patients for a period of three or four weeks and asking them to return for a completion of the treatment. If we have erred at all it has probably been in not pushing the treatment vigorously enough.

From our experience we are entirely disposed to agree with Dreyfus and others in holding that much more harm can be done by giving too little than too much treatment. Most observers agree that the era of excessive individual dosage has passed, and that if salvarsan is properly administered, with due regard to the patient's condition, after a careful examination of the heart, and after ascertaining that the kidneys are normal, the drug can be given repeatedly as outlined above. It is also agreed by practically all authorities, and especially by Ehrlich, that the several contra-indications detailed in the beginning of the salvarsan era have gradually been reduced in number until now it may be said that the only real contra-indications to the injection of the drug are severe renal involvement, very marked cardiac disease with insufficiency of the cardiac muscle, impending coma in diabetes or nephritis, terminal conditions which are not likely to be benefited by salvarsan, and a known intolerance of the drug.

In a very large number of cases treated with salvarsan we have observed very few untoward results. One case developed an enteritis, one a severe nephritis, another an arsenical erythema, and finally, one of our patients developed a lesion in the area supplied

by the inferior cerebellar artery a number of hours after the intravenous injection of 0.3 gram salvarsan. In cases of the kind here narrated that have reacted unfavorably to the injection of the drug the question of further injections has been well considered. In most cases of this type it is possible again to inject the patient after an interval of a few weeks, and after the subsidence of untoward symptoms. Under such conditions it will be best to give not more than 0.15 gram to 0.2 gram to an adult. The injection should be given most carefully, using a concentrated solution (15 to 20 c.c. for salvarsan, 5 to 8 c.c. for neosalvarsan), more especially in cases of vascular disease.

Of the nerve recurrences (neurorecidives) which have been so frequently reported, especially by European writers, we have seen practically nothing. To be sure these are more apt to occur in the early secondary stage of syphilis, which the neurologist infrequently sees, but we question if the early neural involvement is to be attributed to salvarsan treatment properly administered. Some of these cases are surely due to early syphilitic involvement of the nervous system. We know that involvement of the cranial nerves, especially the seventh and eighth, had been described years ago as occurring toward the latter part of the secondary period by Hutchinson, Fournier, Knapp, and others, either before any treatment had been given or after treatment with any of the mercurials. These symptoms are comparable to a neuroretinitis or an iritis, and are specially frequent after insufficient sterilization of the organism by intramuscular injections of mercury or salvarsan, the remaining spirochetes localizing themselves in the poorly vascularized regions traversed by the cranial nerves mentioned above. With the adoption of the intravenous treatment, nerve recurrences have become much less frequent.

The intravenous use of old salvarsan has been so satisfactory in our experience that only recently have we made use of neosalvarsan. On account of the ease of application of this drug and the small quantity of fluid used in its preparation, and because of the less frequent incidence of immediate and remote by-effects, we now use neosalvarsan in doses of from 0.2 gram to 0.6 gram, especially in cases in which a very frequent repetition of the drug is necessary. We have thought it wise in some instances in cases in which it was doubtful if the patient was a good salvarsan risk to begin with the conservative use of neosalvarsan.

The very satisfactory results obtained by the intravenous injection of salvarsan have induced us to resort less often to the intraspinal injections of "salvarsanized serum" as proposed by Swift and Ellis.

According to our present-day conceptions the efficiency test of any antisyphilitic treatment is to be found in the improvement in the subjective and objective symptoms as well as in the change

toward normal in the various biological reactions, viz., Wassermann reaction of the blood and spinal fluid, cytological count, globulin content, and, if we may be permitted to add, the huetin test.

INTRASPINOUS TREATMENT; METHODS. Aside from the fact that the intraspinous methods are all more difficult to perform than the simple intravenous injection, and surely more painful, an analysis of our cases shows that the intravenous injections alone yielded equally good results. For example, in a series of nine cases of tabes that were studied at the Montefiore Home (see Table I), the intravenous injection of salvarsan has accomplished as much for the patient as could be expected from the intraspinous injections combined with the intravenous. From this it is reasonable to conclude that the improvement is due to the intravenous medication.

TABLE I.—Cases of Advanced Tabes.

	Jan. 20 Wasser- mann blood	Jan. 20 cerebro- spinal fluid. Wasser- mann cytology	Salvarsan				Wasser- mann blood. April 15 1914	Wasser- mann cytology. Cerebro- spinal fluid. Apr. 18 1914	
			Jan. 24 1914	Feb. 8 1914	Feb. 24 1914	Mar. 9 1914			
G. D., aged 44	—	+ 80 cells	0.3	0.3	0.3	0.3	—	+ 76 cells	Pain less.
L. G., aged 34	+	+++ 21 cells	0.2	0.3	0.1	0.3	+	+ 4 cells	Pain less.
E. R., aged 48	—	++++ 108 cells	0.3	0.3	0.3	0.3	—	— 9 cells	Pain less; appears markedly impr'd.
M. N., aged 50	+	+++ 35 cells	0.3	0.3	0.3	0.3	+	— 15 cells	Pain less; appears improved.
J. C., aged 42	—	— 35 cells	0.3	0.35	0.3	..	—	— 6 cells	Pain less; impr'd general condition
D. W., aged 51	—	— 15 cells	0.3	0.3	0.3	0.4	+	— 6 cells	First relief from pain in years.
S. D., aged 64	++	+++ 75 cells	0.35	0.3	0.3	..	—	+++ 5 cells	Pain less; general condition impr.
M. G., aged 54	—	+++ 92 cells	0.3	0.4	0.3	Refused puncture	No improvement.
G. F., aged 55	—	...	0.35	0.3	0.3	Puncture impossible	Pain less.
M. F., aged 63	±	30 cells	0.4	0.3	0.4	0.45	—	Cells normal	Improved.

During the past few months we have familiarized ourselves with the injection of solutions of salvarsan and neosalvarsan in minute doses directly into the subdural space of the spinal canal. The procedure was first tried by Wechselmann and by Marinesco, and more recently has been favorably reported upon by Ravaut and others.

For intraspinous administration of these drugs a number of methods may be mentioned. The original methods of Marinesco and of Wechselmann have been modified by Ravaut, who uses a 6 per cent. solution of neosalvarsan in water. Thus if 0.6 gram of the drug were dissolved in 10 c.c. of water, each minim would contain approximately 0.003 gram of neosalvarsan. The needle is introduced as for lumbar puncture, the spinal fluid allowed to run

into the funnel of the apparatus, from one to four drops of the solution are added as desired, and the mixture then allowed to run by gravity into the spinal canal. According to the method of von Schubert, 0.045 neosalvarsan is dissolved in 3 c.c. of water, and of this from 0.1 c.c. to 0.2 c.c. are added to about 3 c.c. of the spinal fluid that has been allowed to gravitate into the funnel. Gennerich avoids what he thinks is an irritative local action of the drug by dissolving 0.15 gram of neosalvarsan in 300 c.c. of water, and injects from 4 c.c. to 6 c.c. of the solution, added to 15 c.c. of the spinal fluid that has gravitated into the injecting funnel.

We have tried these methods and have recently adopted the following method: We dissolve 0.15 gram neosalvarsan in 15 c.c. of freshly distilled water or salt solution. Thus each 0.1 c.c. contains 0.001 gram of neosalvarsan. Of this solution from two to ten or more tenths of a cubic centimeter as desired are added to about 10 c.c. of the patient's spinal fluid. After gently agitating the mixture of spinal fluid and solution in the funnel the fluid is allowed to return slowly into the canal. In this way a minimal amount of fluid (foreign matter) is introduced into the canal. Should further experience prove that this solution is too concentrated it could be made up so that each cubic centimeter would contain one milligram of neosalvarsan.

For the technique of the Swift-Ellis injection of salvarsanized serum the reader is referred to the original publications. Of late some have been tempted to add a few milligrams of salvarsan to the serum before injecting according to this method.

VALUE AND DANGER OF INTRASPINOUS TREATMENT. That all intraspinous injections are not without danger to the patient is evident enough. On a number of occasions after the careful introduction into the canal of salvarsanized serum the patient required opiates to relieve the intense pain. The general condition was also much weakened and the legs partially paralyzed. One patient with early paresis within twenty-four hours after an intraspinous injection of 6 mg. of neosalvarsan developed a complete paralysis of the legs and marked paralysis of the vesical and anal sphincters, the symptoms persisting for three months and leading to death. In another patient with general paresis, three weeks after the sixth intraspinous injection of neosalvarsan, all of the injections having been tolerated without great discomfort, an acute ascending paralysis of the Landry type developed, and death supervened.¹ In view of these facts we have of late hesitated to urge any form of intraspinous treatment.

The various phases of the reaction of the spinal content prove, if they prove anything, that there is an active specific process

¹ Gennerich and others have observed irritative phenomena of lesser degree, such as weakness of the vesical and anal sphincters, shooting pains and areas of anesthesia after intraspinous injections of neosalvarsan in spite of most careful technique.

going on within the cerebrospinal system. The injection of salvarsanized serum is an ingenious and fascinating proposition for which Swift and Ellis deserve great credit, and yet before accepting this method as one of value in the treatment of syphilis of the nervous system the following points should be considered.

It is of the utmost importance to establish the presence of salvarsan or of free arsenic in the blood of patients treated by intravenous injection in order to determine if the use of the so-called salvarsanized serum is based upon rational grounds. It seemed to us that blood withdrawn three-quarters of an hour after an intravenous injection would have to depend for whatever efficiency might be attributed to it upon the presence of the salvarsan itself, since in the short interval (three-quarters of an hour) elapsing between the injection of the drug and the withdrawal of the blood, the organism could not possibly elaborate any form of protective bodies.

We are deeply indebted to Prof. Benedict, of the Cornell Medical School, who made an analysis of ten different specimens of blood which were obtained fifteen to forty-five minutes after intravenous injection of salvarsan, with a view of determining whether or not arsenic was present in appreciable quantities. He was able to detect only 0.00004 gram to 0.0001 gram of metallic arsenic in 20 c.c. of whole blood.

By a simple calculation we have determined that a man weighing about one hundred and fifty pounds, and having a total blood volume of about eight pounds (one-nineteenth of the total weight), if injected with 0.4 gram of salvarsan would have in every cubic centimeter of his blood immediately after the injection, before elimination or fixation by the body cells began, about 0.0001 gram of salvarsan. This is the maximum amount that Benedict has shown to be present in 20 c.c. of whole blood. Thus it is apparent from the analyses of blood taken within three-quarters of an hour after the injection of salvarsan, that the arsenic is not free in the blood-stream, but is probably bound by the receptors of the body cells. Whence it follows that the serum obtained from the blood withdrawn must depend for its efficacy, if it be at all curative, upon some other factor, which has as yet not been determined. If this action depends upon the presence of antibodies in the blood, it would be much more rational to withdraw the blood a day or more after the intravenous injection.

It can be stated also on the authority of Prof. Benedict that from an analysis of four specimens of spinal fluid withdrawn twenty-four hours after an intravenous injection of salvarsan (0.4 gram) the spinal fluid contains free arsenic in about one-sixth to one-tenth the concentration in the whole blood. This is a striking fact and is contrary to the usual belief that none of the drug administered intravenously finds its way into the spinal canal.

It would seem to be proved then that since the blood-serum, which is about one-third the whole blood volume, contains only an infinitesimal trace of arsenic after an intravenous injection of the drug, that the serum as diluted (40 per cent. to 50 per cent.) for intraspinous administration is not truly salvarsanized, and that it contains no more arsenic than does the cerebrospinal fluid after simple intravenous injection. As a matter of fact the spinal fluid actually contains more arsenic than was found to be present in the "salvarsanized" serum, diluted, as used for intraspinous injection. Evidently the recorded biological effects of salvarsanized serum must be due to other coincidental factors, possibly to the intravenous injection of salvarsan and the repeated lumbar puncture.

It is of some interest in this connection to note that in one case (see Table II) the injection of non-salvarsanized (normal) serum reduced the cell count from 302 to 32 cells per cubic millimeter, while the Wassermann reaction remained strongly positive from beginning to end. More recently Dr. Mitchell (in a paper presented before the American Neurological Association) has shown that a similar reduction can be obtained by lumbar puncture frequently repeated.

TABLE II.

J. C., aged 45. Probably general paresis with optic atrophy (blindness).

Blood.	Cerebrospinal fluid.	
Wassermann, +++ March 4, 1914.	Wassermann, ++++ April 11, 1914.	30 c.c. serum intraspinous April 11, 1914.
	Wassermann, ++++ 140 cells c.mm. April 17, 1914.	30 c.c. serum intraspinous April 17, 1914.
	Wassermann, ++++ 128 cells c.mm. April 24, 1914.	30 c.c. serum intraspinous April 24, 1914.
	Wassermann, ++++ 32 cells c.mm. April 30, 1914.	30 c.c. serum intraspinous April 30, 1914.

12.5 c.c. blood-serum diluted with 17.5 normal saline and prepared according to Swift-Ellis method. Serum was obtained from a non-syphilitic patient with negative Wassermann and who had not received salvarsan.

IMPORTANCE OF BIOLOGICAL REACTIONS. Another question which arises in connection with this entire subject is whether a high cell count is a necessary accompaniment of a luetic process and whether the reduction in the number of the cells really is a distinct advantage to the patient and evidence of a change in the basic conditions underlying the morbid process. It is very evident that there is no correspondence between the change in the cell count and the change in the patient's subjective or objective symptoms. Frequently the cell count is reduced but the positive Wassermann test in the spinal fluid persists and is much more difficult to influence, if, indeed, it can be influenced at all in many cases. In cases of tabes both with and without active treatment we have often found a surprisingly low cell count or even a normal

fluid in spite of the persistence of all the clinical features of the case. Then as tabes advances toward its last degenerative stages, there is in most cases a gradual, spontaneous diminution of all the biological phenomena, until finally all the reactions in the spinal fluid may become negative. In a gentleman we have been observing on and off for the past fifteen years, who has an ataxic paraplegia of specific origin, the cell count has been easily reduced to three cells per cubic millimeter by a series of three intravenous salvarsan injections. With this eminently satisfactory condition of the spinal fluid there has been, however, absolutely no improvement in the clinical symptoms. In another case of Erb's type of spinal syphilis the cell count was reduced from 88 cells to 10 cells, and the Wassermann reaction in the spinal fluid became negative, after five injections of salvarsan, but there was not the slightest change in the clinical symptoms. In still another case, though all the reactions became negative in the spinal fluid, the Wassermann remained positive in the blood, and the clinical symptoms were progressive.

We therefore question whether we are not making too much ado over the mere reduction of cells in the chronic cases of central nervous diseases. Where there is a high cell count, and particularly in the more acute luetic processes of the cerebrospinal system, there is no question of the advisability, by all possible means, of attempting to reduce the cell count. But the cell count is merely evidence of the presence of an inflammatory process, and in our enthusiasm over examinations of the spinal fluid do not let us lose sight of the patient.

We have already intimated that there is often very little correspondence between the change in the reactions in the spinal fluid and the change in the clinical symptoms; so let us consider carefully what the general effect of treatment has been on the clinical course of the various classes of cases encountered.

EFFECT OF TREATMENT. 1. As regards *tabes dorsalis*: The most striking effect of the intravenous salvarsan treatment in this condition has been that it has changed what was called a progressive locomotor ataxia into a non-progressive disease in most cases. It has been surprising to notice, particularly in private cases, how little the disease has progressed during several years of observation. In almost every instance the patient has declared that the treatment was doing him good. In the cases treated at the Montefiore Home, all of whom had been under observation for a number of years, under various forms of treatment, and most of whom were very skeptical as to the value of any new form of treatment suggested, the marked subjective improvement was readily acknowledged after salvarsan treatment.

Most of the patients at this institution were constantly receiving the analgesic drugs to reduce the terrific pain incident to the disease

before salvarsan treatment was begun. That this marked betterment in the subjective state of the patient means much in so chronic a disease as tabes goes without saying. While the subjective improvement has been most marked, we have not seen what has been reported by some observers, viz., a change in the cardinal symptoms of the disease. We have not observed a permanent return of the pupillary reflexes nor of the knee-jerk or Achilles reflex. Patients in whom a return of the pupillary function or of the deep reflexes have been observed could, in our opinion, better be designated as cases of cerebrospinal lues of the tabetic type. While we can well claim that the progress of the disease has been stayed in many instances, yet we have had several rather striking experiences tending to show that in spite of early and intensive treatment the progress of an impending tabes could not be averted. Thus a gentleman whose only symptom for many years was an Argyll-Robertson pupil received twelve injections of salvarsan intravenously and innumerable injections of mercury, in spite of which the knee-jerks are growing less lively and lightning pains are making their appearance. A full-fledged tabes will soon be in evidence in spite of all treatment.

If we except the discomfort caused by lumbar puncture and the rather frequent increase in the lightning pains following salvarsan injections for a brief period there is no reason why salvarsan should not be given in every case of this type of disease, no matter at what stage the patient may come under observation, barring, of course, the very terminal period. Years ago one of us had occasion to give anatomical evidence of the fact that there was an active specific process in the bloodvessels of the cord in tabes dorsalis. The studies of the cerebrospinal content together with the anatomical and pathological studies, particularly of French observers, and the more recent findings of the presence of the *Spirocheta pallida* in the cord of tabic patients by Noguchi leave no doubt whatever that tabes is a syphilitic affection, and that only in its later stage can it be considered a parasyphilitic disease. The effect which salvarsan injections have upon the specific process in the spinal meninges is no doubt largely responsible for the marked subjective improvement of patients suffering from locomotor ataxia. But in our enthusiasm over salvarsan treatment, other methods should not be neglected. We wish to emphasize at this point the importance of combining salvarsan injections with the use of mercury, preferably by injections of an insoluble salt. The methods of Fränkel and Förster also should not be neglected. While arrested cases of tabes were occasionally observed before the salvarsan era it must be emphasized that they were not so frequent as they are now under the methods of treatment outlined.

2. As regards *cerebral and cerebrospinal syphilis*, including cases of chronic headache, ophthalmoplegia, and particularly hemiplegia,

it should be noted that the improvement after salvarsan treatment has been most satisfactory. Headache and ocular palsies, and even specific spondylitis, have disappeared more rapidly than under any previous form of treatment. That recovery is more rapid and more complete in hemiplegia we have also been able to record. Little more need be said on this subject than that in these cases the syphilitic process is an active one affecting the bloodvessels and the meninges chiefly, and for this reason, it may be, the salvarsan has been more effective.

We desire also to refer to several cases of optic neuritis of distinctly specific origin which we have had occasion to observe. Inasmuch as there has been at all times considerable fear of active antilucetic treatment in cases of optic neuritis, it is particularly important to emphasize the fact that energetic salvarsan treatment has been productive of excellent results, and what was feared to be a most serious condition of the optic nerves has been recovered from under this treatment. The following case in point is cited:

B. R., aged twenty-five years, single, admitted to hospital September 1, 1912. Had chancre in May, 1912. One intravenous injection of salvarsan in June followed by injections of mercury. In the beginning of August began to suffer from headaches and vomiting. About the middle of the month he noted that his right arm was becoming weak and that his eyesight was failing. His condition became progressively worse and diplopia developed. After admission to the hospital he had convulsions, affecting principally the left side. Mental state confused. Rigidity and retraction of head. Kernig's sign present. Examination of the fundi showed bilateral choked disk of three to four diopters and hemorrhage and exudate in the disk and macular region. He was treated as follows:

CASE.—B. R.

September 1, 1912. Salvarsan, 0.3. Wassermann +, blood and spinal fluid.

September 10, 1912. Salvarsan, 0.3.

September 17, 1912. Salvarsan, 0.3.

September 27, 1912. Salvarsan, 0.3.

October 4, 1912. Discharged. Optic neuritis much improved.

April 7, 1913. Readmitted. Wassermann weakly + in blood; positive in spinal fluid. 25 lymphocytes per c.mm.

May 6, 1913. Salvarsan, 0.3. Wassermann + spinal fluid. 80 cells per c.mm.

May 22, 1914. Wassermann: Negative in blood and spinal fluid. 2 cells per c.mm. Globulin: negative.

Received fourteen injections of salvarsan 0.3 to 0.4 gram and a number of injections of mercury salicylate.

At present his fundi show a postneuritic atrophy, but he has 20/20 vision in one eye and 20/30 vision in the other. There are no symptoms of any other organic lesion.

We have also had cases of tabes with optic atrophy in which the atrophy has progressed in spite of salvarsan treatment; but cases of this type should not be held to militate against the administration of salvarsan in active optic neuritis of syphilitic origin. That some such cases have gone on to blindness is unfortunately true, but however inclined to pessimism we may be, we cannot attribute such blindness to the salvarsan, nor are we willing to admit that the loss of vision and complete blindness were hastened by the use of the drug.

Here is a second case in point:

L. D., aged twenty years. Admitted to the hospital in April, 1913. She gave a history of severe headaches, vomiting, failing vision, and convulsions of Jacksonian type. Examination revealed well-marked, bilateral choked disks; Wassermann reaction negative in both blood and spinal fluid; cells only slightly increased. Salvarsan 0.25 gram given without relief. Exploratory craniotomy then performed. No tumor found, but the meninges appeared to be thickened and the seat of a chronic inflammatory process. Following the operation there was relief of symptoms until August, when she was readmitted because of the reappearance of the headaches and convulsions. The increase of cells in the spinal fluid then indicated a syphilitic process, and salvarsan was continued as shown in the case of B. R., with good effect.

It is interesting to note the increase in the cells of the spinal fluids before the Wassermann became positive, and the appearance of the reaction in the blood and spinal fluid after the administration of a considerable quantity of salvarsan. This is an example of a "provocative reaction." It is important to note that an examination of the blood of the father showed a positive reaction.

CASE L. D.—Cerebral lues (congenital).

April 10, 1913. Cerebrospinal fluid: Wassermann, —. Cells slightly increased.

April 11. Salvarsan, 0.25; intravenous. Symptoms pointed to neoplasm. Exploratory craniotomy.

April 23. Blood: Wassermann, —.

August 9. Cerebrospinal fluid: Wassermann, + (?); twenty-five cells.

October 4. Cerebrospinal fluid: Twenty-five cells.

October 8. Neosalvarsan, 0.45.

October 15. Salvarsan, 0.2. Cerebrospinal fluid: Wassermann, +. Pressure, 320 to 380 mm. Forty-one cells cubic millimeter.

November 11. Blood: Wassermann, —.

November 25. Salvarsan, 0.3, and intraspinal.

December 8. Cerebrospinal fluid: Wassermann, —. Ten cells. Globulin, ++.

December 8. Salvarsan, 0.3; intraspinal, 30 c.c.

February 9, 1914. Salvarsan, 0.3; intravenous. Cerebrospinal fluid: Wassermann, ++. Globulin, +. Twenty-four cells. Pressure, 400 mm.

February 14, 17, 19. Convulsions.

March 10, 14, 18. Neosalvarsan, 0.6.

Still another patient presented diplopia and bilateral choked disks, and after receiving four injections of salvarsan intravenously made a complete recovery within a few weeks.

3. Finally, let us consider briefly the results of treatment in cases of *general paresis*. There is no longer doubt of the syphilitic nature of this disease since the discovery in the cortex of the brain by Noguchi and Moore of the *Treponema pallida*. And it may be that the ineffectiveness of our treatment up to date has been due to the fact that the salvarsan does not reach the organisms in sufficient concentration by our present methods of administration to destroy them, or that they are very resistant and that some other agent or method will have to be discovered potent enough to kill them. The fact remains that thus far we have been unable to cure a single parietic, nor are we inclined to the belief that anyone has effected a cure in an undoubted case of general paresis.

We have succeeded in arresting the disease in its early stages, temporarily in a few cases, by giving frequent doses of salvarsan intravenously. In one case of taboparesis of long duration in which the patient had developed well-marked delusions of grandeur with maniacal excitement, incontinence of urine and feces, and had a large bed-sore, the effect of the intravenous administration of the drug was truly marvellous. But it must be recorded that in the earlier period of his disease the use of mercurial injections alone had been followed by a remission. The occurrence of spontaneous remissions in this disease makes it difficult to judge of the efficacy of any form of treatment.

On the other hand we have seen some cases that not only have progressed steadily during the course of treatment, but in some instances the fatal termination seemed to have been hastened by it. We favor the use of salvarsan in general paresis, in the hope of bringing about periods of remission. Until we find an adequate substitute, salvarsan should be administered vigorously and at the earliest possible stage of the disease. The cure of general paresis is a problem for the future; its solution may be reached by further careful experimentation.

CONCLUSIONS. The most remarkable recent achievements in the treatment of syphilis of the nervous system are due to the possibilities of earlier recognition of all forms of syphilitic disease. Wherever there is a strong suspicion of syphilis, and particularly if there is corroboration of the diagnosis by examination of the blood and of the cerebrospinal content, and even in the absence of such corroboration, most intensive salvarsan treatment should be

instituted. Under the ordinary precautions such treatment will do no harm and may be productive of great good. In *tabes dorsalis* the subjective condition of the patient can be greatly improved and the progress of the disease checked. In all cases of cerebral and cerebrospinal lues the salvarsan treatment combined with mercury accomplishes more than we were able to accomplish by any previous methods. The intravenous injection of salvarsan has been in our opinion the most satisfactory form of treatment. The intraspinal treatment possesses no advantage over the intravenous. We have shown definitely that the "salvarsanized" serum contains an infinitesimal trace of arsenic and too little to be of any therapeutic value. The spinal fluid contains as much arsenic as does the "salvarsanized" serum. Up to the present time the results in general paresis have been the least satisfactory, but there is some reason to think that by the more careful elaboration of therapeutic methods more satisfactory results will be within reach.

CARDIAC SYPHILIS: REPORT OF CASE.¹

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THIS subject was called to the attention of the writer by the comprehensive article by Professor Harlow Brooks in the October, 1913, number of this JOURNAL.

Shortly before the article was received here the autopsy occurred of a case of syphilitic myocarditis complicating a quiescent pulmonary tuberculosis of small degree. In view of the fact that this patient had refused all antiluetic treatment the findings histologically are thought to be of exceptional interest and worthy of report as a sequel to the paper of Professor Brooks.

Case No. 4412, admitted June 2, 1911, for pulmonary tuberculosis. Duration of disease given as seven months.

Previous History. Typhoid fever in 1889; malaria, in 1908; primary syphilis in April, 1907, for which the patient received twenty-two months' mercurial and eight months' potassium iodide treatment. No relapses. Wassermann positive in 1911.

At admission his tuberculous activity was slight and the diagnosis was active tuberculous involvement of the upper parts of both upper lobes. Tubercle bacilli were found in the sputum.

¹ Published with the permission of the Surgeon General, United States Army.

In September, 1911, the tuberculous activity continued and in addition the patient complained of transient pain over the precordium and anterior left chest.

January, 1912, the patient had a slight hemorrhage.

May 1, 1912, the lung condition is recorded as inactive.

May 25, 1912, the patient had asthmatic attacks at night. Sputum was blood-streaked and the lungs contained considerable moisture, which was recorded as due to passive congestion rather than tuberculous activity. Apex of heart just outside the left mammary line in the fifth interspace. Heart action feeble and irregular. Pulse small and wiry and of high tension.

From this time to January, 1913, the patient seemed to improve, but in this month was confined to his bed because of severe asthmatic symptoms. Blood examination showed only 3 per cent. eosinophiles.

In March, 1913, the heart dulness began at the second rib left and fourth right and extended two fingers' breadth to the right of the sternum and to the eighth rib in the midaxillary line in the left.

All heart sounds muffled. Sternum extremely sore at the level of the fifth interspace. Paracentesis of the pericardium failed to show fluid. Urine contained casts but no albumin.

Left the hospital improved to a slight degree in July and was readmitted one month later. At this time he complained of smothering attacks, necessitating his sitting up at night. Heart area as at the examination in March, 1913. Signs were similar except that a normal and low tension beat regularly alternated. Urine contained both albumin and casts.

October, 1913, Wassermann was positive.

In November edema of the lower extremities developed. During December the patient failed rapidly, expectorated considerable blood as a result of the passive congestion, and the kidney condition increased in severity. Edema increasing. In the early part of the month there occurred a thrombosis of the left subclavian vein at its junction with the internal jugular, and in consequence the left arm became markedly swollen and painful. Death December 28, 1913.

EXTRACTS FROM THE AUTOPSY PROTOCOL. *General.* Edema of moderate degree of both lower extremities. Left arm is markedly swollen and edematous. Thrombus at the junction of the left subclavian and internal jugular veins, which is partially organized and completely obliterates both vessels.

Heart. Weight, 690 grams; is free in pericardium, which contains 200 c.c. of a clear amber fluid. Heart chambers and great vessels are distended with dark red, moist clots. The coronary arteries are, in places, partially obliterated by atheromatous patches, which show, beginning softening. The heart muscle is increased in thickness and is pale and edematous. A lighter tissue

is rather irregularly distributed throughout the myocardium, but is more abundant in the muscle of the interventricular septum. In both ventricles there is a loss of endothelium at the apices over the lower fourth of the interventricular septum, and here the walls are covered with an adherent, partially organized thrombus. The epicardium shows several whitish, opaque edematous areas from 0.5 to 1.5 cm. in diameter, slightly raised above the surface. Beneath these areas the tissue is pale and swollen and extends, gradually decreasing in extent, to the endocardium.

MICROSCOPIC EXAMINATION. The muscle of the left ventricle shows, universally, an atrophy of the muscle cells with a deposit of brown pigment about the nuclei, irregular in its distribution. The nuclei show an apparent increase in size and number. Replacing the shrinkage in muscle is a general increase in connective tissue infiltrated with lymphocytes and endothelial leukocytes. In places this tissue completely replaces areas of muscle, and these replacements vary from dense fibrillar to loose areolar tissue, with relatively few fibrillæ, in which endothelial leukocytes predominate over lymphocytes and there are many young connective-tissue cells. This loose tissue either is present exclusively or surrounds the fibrillar, and the latter instances represent the advance of the process of replacement of muscle. At these advancing borders and included in the areolar tissue the muscle cells are extremely atrophic and many have no nuclei while the striations are blurred and indistinct.

Many of the vessels show a subendothelial proliferation of the intimal connective tissue and a few of the smaller ones are obliterated by this process.

In some of the sections the endocardium is absent and the surface is covered with clot showing beginning extension of connective-tissue processes into it.

The changes in the muscle of the right ventricle are of the same type, though the muscle cells, as a whole, are degenerated to a more advanced degree than those of the left heart. The distribution of the connective tissue is more regular and less of the young areolar type is present.

Other conditions found present at autopsy were degenerative and productive nephritis (Oertel); general chronic passive hyperemia; general arterial and venous subendothelial proliferation of the intima, probably of syphilitic origin, though treponemata were not demonstrated; a small amount of apparently inactive tuberculosis of both apices.

Death was due to pulmonary embolism, with hemorrhagic infarction of the lungs.

For the discussion of the subject in general the reader is referred to the article of Professor Brooks, which admirably covers the ground.

As regard individual peculiarities this case during the latter part of the disease presented the regular occurrence of alternate high and low tension cardiac beats where, as Brooks says, the characteristic of the arrhythmia in these cases is its irregularity.

Runeberg has observed a 'muffling or tonelessness of the first sound at the apex which was present in this case.

The microscopic findings show an active advance of the process and indicate the course of the disease without treatment and for this reason are especially interesting.

The connective-tissue proliferation was of the type of the diseases known as infectious granulomata; that is, an avascular new growth of connective-tissue found in leprosy, tuberculosis, etc., as well as in syphilis.

In conclusion the writer wishes to tender his thanks to Captain Robert C. Loving, Medical Corps, United States Army, to whom he is indebted for the clinical observations and remarks.

DUODENAL ULCERS IN INFANCY.

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DURING a period of two years 5 cases of duodenal ulcer have been seen at the St. Louis Children's Hospital. In 4 of the cases a clinical diagnosis was made which was later confirmed in 3 instances at autopsy, and in but 1 case was the lesion unsuspected during life and found postmortem. In the fourth case in which the diagnosis was made the infant recovered. As the cases of duodenal ulcer in infancy which have been reported have been, with one or two exceptions, cases in which the lesion was an autopsy finding and unsuspected clinically, our series of cases has been of unusual interest, as we have been able to observe the clinical condition more closely than is possible from a postmortem view-point.

In a recent paper in which most of the reported cases are briefly recorded, Holt¹ was able to find 91 cases of duodenal ulcer in the first year of life in literature, to which he added 4 cases from a total of 1800 autopsies at the Babies' Hospital in New York; 9 of these cases collected by Holt are more strictly cases of melena neonatorum, and from a stand-point of pathogenesis the propriety of their inclusion with the remaining cases is a debatable question. Including

¹ Amer. Jour. Dis. Child., 1913, vi, 381.

the 4 cases of Dr. Holt and the 5 of our series it makes in all a total of only 100 cases in literature, of which 80 per cent. have been reported in the last six years. Previous to this time the cases reported were mostly single case reports, and in large part had to do with ulcers in the newborn infant associated with melena. In 1909 Helmholz² reported 8 cases of duodenal ulcer in infants with "pedatrophie" which he had found in 16 autopsies at the Berlin Kinderasyl. Since Helmholz's paper called attention to the condition, a number of cases and series of cases have been reported, but with a few exceptions they have had to do with pathological findings and in not more than four cases has the condition been diagnosed before death.

It is difficult to judge of the frequency of the condition. Helmholz, as noted above, found 8 cases in 16 autopsies, but in 4 of the 8 the ulcerations were superficial. In a second paper³ the incidence was very much less. Entz,⁴ in Budapest, found 10 cases in 364 autopsies on infants, and Schmidt,⁵ from Breslau, reported 20 cases in 1109 autopsies. Holt⁶ found 4 in 1800 autopsies of which 90 per cent. were in children under one year. The condition is unquestionably much more common than reported by the last two observers. Our own experience is interesting in connection with the irregularity in statistics. In 1910 we found an ulcer at autopsy in the case reported by Griffith,⁷ and subsequently for a period of two years carefully examined the cases of atrophic infants coming to autopsy at three Philadelphia hospitals without finding a second case, nor were any cases seen clinically during this time in which the condition was suggested. During the last two years, however, 5 cases were seen at one hospital in St. Louis. From a pathological stand-point the condition was found 4 times in 62 autopsies on infants under one year. From a clinical stand-point the diagnosis was made 4 times in a total of 586 admissions to the infant ward and 2000 infants under one year passing through the out-patient clinic. The histories of the five cases are briefly as follows:

CASE I.—No. 2636, T. R., a female infant of one month, was admitted March 20, 1912. Family history negative. Full-term baby, said to have weighed eight pounds at birth. Breast-fed for two days and then given condensed milk 1 to 16. This was taken well for two weeks, although there were two or three stools a day, but for two weeks before admission the infant had been refusing her feedings and the stools had become loose and watery. Two days before admission she was brought to the out-patient clinic, where she was put on barley water. This was refused, and on her return two days later she was admitted to the ward. There had been a rapid loss of weight the week before admission.

² Deutsch. med. Woch., 1909, i, 534.

³ Helmholz, Arch. Pediat., 1909, xxvi, 661.

⁴ Entz, quoted by Fleisch, Jahrb. f. Kinderh., 1912, lxxvi, 542.

⁵ Berlin Klin. Woch., 1913, I, 593.

⁷ New York Med. Jour., 1911, xciv, 572.

⁶ Loc. cit.

Weight on admission 2550 gms. Except for the typical picture of alimentary decomposition there was nothing of importance in the physical examination. On the day of admission four loose mucous stools were passed and the infant vomited once. She was given one-fourth milk without sugar, but the stools failed to improve, and even this weak food was vomited occasionally. A change was then made to protein milk, but it was without effect, and a continuous loss of weight occurred while the infant was in the hospital.

On March 30, ten days after admission, a quantity of black granular material was vomited, and shortly afterward a black tarry stool was passed. The temperature remained continuously subnormal, but no evidences of collapse developed. A diagnosis of duodenal ulcer was made from these symptoms.

Two days later more tarry stools were passed, which, like the previous stool, gave positive blood tests. The infant gradually became weaker and weaker, and died three days later, on April 5.

An *autopsy* by Dr. George M. Smith showed an irregular ulcer 7.5 x 5 mm., situated on the posterior wall of the first portion of the duodenum just beyond the pylorus. The margins were elevated and undermined. A second ulcer 3 mm. in diameter was present 0.5 cm. below the first. The ulcers extended through the mucosa and submucosa, and their bases were covered with a grayish slough. No other lesions of importance were found.

CASE II.—No. 4026, V. Y., a female infant of five months, was admitted March 11, 1913. Family history negative. Full-term infant, and said to have weighed six pounds at birth. Breast-fed for two months, when a change was made, as she failed to gain in weight and "refused to nurse." There was occasional vomiting while on the breast. After the breast-feeding, malted milk, cow's milk, "Nestlé's Food," "Mellin's Food," and cow's milk for a second time were tried in turn. All were vomited or regurgitated, and the infant failed to gain. For two weeks before admission whole cow's milk plus sugar and lime water had been given in indefinite quantities. Constipation had been more or less constant since birth, and cathartics had been freely used.

The physical examination on admission showed a markedly emaciated infant weighing 3000 gms. Nothing of importance was noted outside of the picture of severe decomposition.

The infant was admitted late in the afternoon of March 11. Early the following morning there was a sudden collapse, requiring considerable stimulation, which was followed by a rise of the temperature to 103°, and some hours later during the evening a tarry, semiformed stool was passed which gave a positive blood-test. From the collapse followed by the passing of a tarry stool a diagnosis of duodenal ulcer was made.

Breast milk was given, but was vomited and blood appeared in the vomitus. Severe prostration developed and the infant died

two days later, March 14, after passing a second large tarry stool. Except for the vomiting there were no signs pointing toward a pyloric obstruction (tumor, peristalsis).

At the *autopsy* by Dr. Smith the pylorus was found slightly thickened and tightly contracted, but there was no hyperplasia of the muscle bundles. 8 mm. beyond the pyloric ring, on the posterior wall of the first portion of the duodenum, there was an irregularly triangular-shaped ulcer 1 x 0.5 cm. The edges were sharp and clean cut and the base of the ulcer was grayish and bile-stained. Four small areas of bile, stained superficial necrosis were present between the lower edge of the ulcer and the ampulla of Vater. No other lesions of interest were found.

CASE III.—No. 4080, R. H., a male infant of three months, was admitted March 24, 1913. Full-term baby weighing six and a half pounds at birth. Family history negative. Breast-fed for one month, when a change was made to a cow's milk mixture (2.5-7-1.3). This was vomited, and after three weeks a change was made to Horlick's milk on the advice of a druggist, which was continued until the time of admission. Nevertheless the infant continued to lose weight and the vomiting persisted, becoming quite severe the week before admission. The stools passed a day or so before admission were black and tarry.

The physical examination on admission showed an infant weighing 2800 gms., markedly emaciated and prostrated. Vomiting was severe and the stools were black and tarry. From the history and condition at time of admission a diagnosis of duodenal ulcer was made.

All food was withheld for thirty-six hours and fluids maintained by hypodermoclysis. A milk mixture (2-7-1, 8 x 50 c.c.) was then given for five days and then increased in quantity as the vomiting became less. The stools improved, and although no further gross evidences of blood were seen occult blood tests were positive for a period of two weeks. About three weeks after admission we were able to obtain a wet-nurse for the baby and from this time on improvement was rapid. A week later the infant was discharged from the ward and the feeding and care supervised from the out clinic. No further gastro-intestinal lesions developed. Some ten months later when the nutritional disturbance had apparently been entirely cured the infant died of pneumonia. He was treated at home for this illness and was under the care of a private physician, hence we were unable to obtain an autopsy.

CASE IV.—No. 6406, J. R., a male infant of three months, was admitted February 7, 1914. Family history negative. Full-term baby, said to have weighed eight pounds at birth. Breast-fed for two months, and then put on half milk and half oatmeal water with lactose added, which was continued until the time of admission. The infant failed to gain weight satisfactorily on the breast and lost

weight on the cow's milk feeding. The cow's milk was not taken well, and at times there was a little vomiting. The stools were constipated.

Physical examination showed a poorly developed and undernourished infant weighing 3700 gms. Nothing else of importance noted. There was a severe and persistent vomiting after admission, lasting for three weeks, which did not respond to a decrease in both the quantity and strength of the food and was but little influenced by lavage. No signs of pyloric obstruction were observed during this time. The infant lost 400 grams during this period, and developed a rather persistent furunculosis, from which cultures of staphylococci were obtained.

On the night of February 28, three weeks after admission, the infant suddenly collapsed and shortly afterward a stool containing considerable blood was passed. From these symptoms a diagnosis of duodenal ulcer was made.

The feeding was at once changed to breast milk obtained from a wet-nurse, and for a month the infant's condition remained practically stationary. At times occult blood tests on the stools were positive, but no further gross amounts of blood were passed until one month later, March 28, when black, tarry stools were passed which gave a marked guaiac test. The following morning the infant died.

At *autopsy* by Dr. Smith an ulcer 0.3 cm. in diameter was found on the posterior wall of the duodenum, midway between the pylorus and ampulla of Vater. The ulcer was "punched out" with elevated margins and extended to the serous coat of the intestine. Nothing else of importance was present.

CASE V.—No. 6617, D. W., a female infant of two months, was admitted March 26, 1914, and died three weeks later on April 17, 1914. Family history was negative. Full-term baby weighing seven pounds at birth. Breast-fed for two weeks and then given condensed milk for a month. For the two weeks previous to admission a mixture of cream 4 ounces, water 13 ounces, lactose $\frac{1}{2}$ ounce had been given. Since the infant was two weeks old she had vomited regularly several times a day and had never gained weight. The stools were constipated when on the condensed milk but for a short time before admission they had been more frequent and "lumpy," but no blood or mucus had been observed.

Physical examination showed an infant of 2500 grams with the typical picture of alimentary decomposition. While in the hospital breast milk from a wet-nurse was given, but no improvement took place. The stools were never normal, but at no time did they show any gross evidences of blood. The case was regarded as one of uncomplicated decomposition, and no occult blood tests were made on the feces. The infant vomited a few times when in the hospital, but this was not a noticeable feature of the case.

Autopsy.—Just below the pylorus, occupying the posterior superior part of the duodenum, there was a round punched-out ulcer measuring 0.5 cm. x 6 mm. in height x 4 mm. in depth. The edges were sharp, thick, and smooth. The base was grayish yellow in color and bile-stained. Two small superficial ulcerations situated 0.5 cm. and 0.75 cm., below the ulcer described, were present, which appeared to be recent and were also bile-stained. The rest of the intestinal tract showed no gross lesions.

SYMPTOMATOLOGY. It will be noted that the first four of our five cases presented a fairly typical picture, from which we were able to make a diagnosis that was later confirmed at autopsy in the three fatal cases. In the fifth case the history was somewhat suggestive from a retrospective view-point, but the essential symptom upon which a diagnosis must be based was not observed. Taking up the symptoms in detail it will be noted that all of the infants were under six months of age and "marasmic." As the factor of diet plays such an important part in the production of alimentary decomposition it is interesting to note that three of the infants received a fair start on breast milk, and that in only one case were the diatetic errors pronounced. In other words the degree of the chronic nutritional disorder was out of proportion to the diatetic fault. In none of the cases had there been an acute gastro-intestinal disturbance.

A second symptom present in all five of our cases was vomiting. This was given as a marked feature in the histories of three of the cases and as an occasional occurrence in the other two. In one of these two, however (Case IV), the vomiting was severe and persistent while the infant was in the hospital. Vomiting is reported as being present in many of the cases whose clinical history is recorded and in some was very severe. In a few cases, as in our fourth, the vomiting has closely resembled the type occurring in pyloric obstruction and in all probability the mechanism is to a large extent the same, the ulcer situated just beyond the pylorus acting as an irritant, producing a spasm of the pylorus. The remaining symptoms of pyloric stenosis, peristaltic waves and tumor, were absent in our cases, but were observed by Torday⁸ in a case of duodenal ulcer, although no stenosis was found at autopsy. In Case II of our series the pylorus was found tightly contracted at autopsy, but there was no hypertrophy of the muscle bundles present.

There is, to be sure, nothing very unusual in the association of vomiting and decomposition, but when, in the absence of acute ulcerative lesions of the large intestine and other conditions as a polyp which cause hemorrhage, massive hemorrhage from the bowel is added, the symptoms are strikingly suggestive of duodenal ulcer if not pathognomonic. Holt⁹ found that bloody stools were ob-

⁸ Torday, *Jahrb. f. Kinderh.*, 1906., lxiii, 563.

⁹ *Loc. cit.*

served in 28 of 64 cases in which the clinical histories were recorded and they were present in 2 of his 4 cases. In our series massive hemorrhage was present in 4 of the 5 cases, and if the case reported by Griffith is added, in 5 of the 6 cases which have come under my personal observation, a much higher percentage than in the cases collected by Holt. As the blood may be largely digested by the time it is passed, it is not at all improbable that hemorrhages may have been overlooked in some of the reported cases, particularly in cases from institutions where a daily inspection of the stools by the medical staff is not a part of the routine. The fourth case of our series in which there were two massive hemorrhages a month apart illustrates another phase of the question of hemorrhage. In the interim, although no gross evidences of blood were present, we were able to demonstrate the presence of blood in the stool by occult blood tests. Occult blood tests were also positive in Case III for some time after the tarry stools had been passed. It is possible in this way that a diagnosis may be made without gross evidences of blood. We have made occult blood tests on the stools of a few cases of decomposition with as yet uniformly negative results. If the infant is vomiting at the time of a large hemorrhage, blood will usually appear in the vomitus as in Case II.

Severe collapse has occurred in many cases accompanying and as a result of hemorrhage and in some cases has apparently been the direct cause of death. The degree of collapse is naturally dependent upon different factors as the condition of the infant at the time of the hemorrhage and the amount of blood lost. In Case I it was a minor factor while in Case IV it was almost immediately fatal. In this case it was some hours before the passing of a bloody stool and in several of the reported cases in which death occurred in collapse, hemorrhage was first found at autopsy in the form of blood-clots in the lumen of the intestine.

DIAGNOSIS. The absence of subjective symptoms which are of so much value in the diagnosis of duodenal ulcer in the adult make the diagnosis dependent upon the association of the few objective symptoms described above. The presence of gross hemorrhage is the only definite symptom pointing to a duodenal ulcer, and hence when this symptom, which may be looked upon as a complication, is absent the diagnosis cannot be made. It is of course essential to exclude acute ulcerative lesions of the lower intestine, anal fissure, etc., but these causes of hemorrhage are usually associated with acute nutritional disturbances and are easily differentiated. Whether or not a diagnosis can be made by the use of occult blood tests when no gross evidences of hemorrhage have been observed is a question to be determined. That such tests should be made in all cases where vomiting is associated with atrophy in young infants is indicated, as it is only in this way that the value of such tests for the early diagnosis of duodenal ulcer can be determined. Our

series of cases, in which the diagnosis was confirmed at autopsy in the three fatal cases in which a clinical diagnosis was made, shows that it is possible to make the diagnosis with a high degree of certainty when the symptoms described above are present. We have not had any cases in which the condition was suspected and not found at autopsy.

Holt¹⁰ in the second case of his series used a duodenal catheter (this case had a coincident jaundice) and twice found blood in the tube. From this, together with the presence of blood in the stools, the clinical diagnosis of duodenal ulcer was made. He recognizes the possible harmfulness of this procedure, but thinks that the risk is so slight that it may be ignored, and recommends the use of the duodenal catheter for purposes of diagnosis. We have had no experience with the duodenal catheter, but from the anatomical condition of some of the ulcers we have observed, and as in all probability some ulcers heal if let alone, we would not personally care to use the catheter if we suspected the presence of a duodenal ulcer.

PROGNOSIS. The data from which practically all our knowledge of the condition has been obtained must be taken into consideration in any discussion of the prognosis. Up to the present time it has been a lesion found almost entirely postmortem and unrecognized clinically. This is not a proof that the lesion does not occur more frequently than autopsy figures would indicate, and is followed by healing. Helmholtz¹¹ reported a case in which recovery followed fairly typical symptoms, and Case III of our series makes a second case in which the group of symptoms pointing to an ulcer of the duodenum has been recognized clinically and the infant recovered. In a case reported by Schmidt a scar of an old duodenal ulcer was found at autopsy in an infant of five months. The ulcer in Case V of our series was of a distinctly chronic type. The prognosis must be looked upon as unfavorable, however, and this in large part is due to the age of the infants in whom the ulcers are most frequently found and the association of chronic nutritional disorders.

TREATMENT. Very little can be said in regard to the treatment of a condition about which so little is known. About the only indication is to place the infant under the best nutritional conditions, which means breast milk, and it is to this alone that we attribute the improvement in Case III. Surgical interference has not been deemed advisable in any of our cases, owing to the severe general nutritional disorder of the infants at the time the diagnosis was made. If methods are found by which an ulcer can be recognized early, surgical treatment offers at least a theoretical possibility.

PATHOGENESIS. The question of etiology and pathogenesis has been left to the last, as except for the pure morbid anatomy of the ulcers the pathology of the condition is obscure. A few associated

¹⁰ Loc. cit.

¹¹ Loc. cit.

phenomena are of interest, and probably of importance, but any deductions made from them are still of the nature of hypotheses.

The ulcers may be either single and multiple, and vary from small areas of superficial necrosis to cleanly "punched-out" ulcers, which involve all of the layers of the intestinal wall, and which in a few cases have even perforated with a resulting peritonitis. They are found between the pylorus and ampulla of Vater, and are most commonly situated just beyond the pyloric ring. In all four of our cases which came to autopsy the ulcer was located on the posterior wall, and this is true of practically all of the cases reported in literature. The few exceptions are in duodenal ulcers of the newborn. Whether or not this has any relationship to the origin of the ulcers is uncertain, but my attention was called by Dr. George M. Smith to the fact that this (the posterior wall) would be the most dependent part of the duodenum with an infant upon its back, and hence for mechanical reasons the point upon which any substance acting upon the mucosa would be most apt to exert its action. From a pathological stand-point care must be taken to distinguish the early stages of true ulceration with inflammatory reaction from the superficial necrosis (digestion) which develops with exceeding rapidity postmortem or shortly before death.

Little is known of the conditions leading to the development of duodenal ulcer in the adult. Most theories presuppose a lowered integrity of or some insult to the cells of the mucosa, with subsequent action of gastric or intestinal secretions. Arteriosclerotic changes do not come into the question of the development of ulcers in infancy, and whether the same factors are at work in the production of ulcers in both the infant and adult is a matter of conjecture. That the ulcers in infancy may be present for some length of time and thus have a certain chronicity is shown by Case IV in our series. Healing may occur as is shown by the case of Schmidt's mentioned above, by Case III in our series, and the case of Helmholz, which recovered. It is not at all unlikely that many cases of duodenal ulcer develop and later heal, being unrecognized clinically.

The age at which duodenal ulcers are found is of interest as the lesion seems to be almost entirely restricted to early infancy. They occur most frequently between the first and fourth months and only 5 out of 65 cases according to Holt have been reported in infants over five months. The ages of the patients in our series, one, five, three, three, and two months respectively, are in agreement with this age incidence. This is the same age period at which alimentary decomposition most frequently develops, and the association of chronic nutritional disease with duodenal ulcer is considered by some as of more than casual importance. Helmholz¹² who reported the first series of cases took as the theme of his paper the association of

¹² Loc cit.

duodenal ulcer with "pedatrophie." Finklestein,¹³ who so far as we know is the only author of a text-book of pediatrics who has given the subject any consideration, considers the tendency to ulceration to have its origin in the processes of decomposition.¹⁴ It is on the other hand as easy to defend the view that the decomposition is a result rather than a cause of duodenal ulcer, and hence that duodenal ulcer is one of the many causes of chronic nutritional disease, or that both are dependent upon the same causes. The cases of duodenal ulcer in the newborn and the few cases of ulcer in infants without chronic nutritional disorders would point toward these latter conceptions. Whether the relationship of the nutritional disorder to the duodenal ulcer is one of cause or result the association of the two is one of the most striking features of the pathology and is a factor of importance in the diagnosis, prognosis, and treatment.

EFFECTS OF HEREDITY IN BOVINE TUBERCULOSIS.¹

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THAT a very high percentage of dairy cattle are tuberculous, that is, are "reactors" is a universally admitted fact. State and municipal laws are more and more insisting that the milk of tuberculous animals shall not be sold, and the question of bovine tuberculosis has become a serious economic as well as hygienic problem. When one realizes that for general use milk must be furnished at a rate which can be paid by the average citizen and at the same time appreciates the fact that the dairyman must expect from 15 to 50 per cent. of his stock to be ruled out if the tuberculin tests are rigidly enforced, the problem of milk supply becomes a factor of very great difficulty as well as importance. A further fact of great bearing is the strong probability that the more highly blooded cattle are most likely to be found to be reactors. This makes the problem of the honest and ambitious dairyman even more difficult, for if he attempt to increase the quality of milk or the butter production of his herd, he almost invariably breeds in tuberculous stock, and unless extraordinary and expensive methods of isolation are practised dissemination of the infection is almost certain to follow. On

¹³ Lehrbuch der Sauglingskrankheiten, Zweite Hälfte, p. 206.

¹⁴ In nicht allzu seltenen Fällen kommt es zu teerfarbenen Entleerungen als Symptom von Darmblutungen. Sie stammen aus peptischen Duodenalgeschwüren, die sich nach neuen Feststellungen bei dekomponierten Kindern so häufig finden, dass der Dekompositionsvorgang in irgendeiner bisher noch dunklen Weise die Disposition dazu begründen muss.

¹ Read before the Association of American Physicians, May 13, 1914.

the other hand, if he fails to thus improve his stock he is very likely to get into trouble because the quality of his milk may be found deficient and he thus also lays himself liable to prosecution.

The difficulty of improving breed is a very serious matter, particularly for the farmer of small capital since the price of blooded stock is always high and he is very likely to purchase as non-reactors cattle which have been "plugged" against the tuberculin reaction by dishonest dealers. This trick of "plugging," though familiar to most stock men, I find is not widely known by physicians. There is no doubt but that when tuberculin tests are known to be about to be made, this method is practised so that negative results are obtained even in cattle which may be extensively so diseased. "Plugging" is performed by injecting a dose of tuberculin a few days before the public or legal test. For some time after the reaction which follows this injection, subsequent tuberculin tests are negative so that even widely diseased animals may be tested and sold apparently as free from tuberculosis. As can be seen, detection of this fraud may be practically impossible.

Another point often unrecognized by the hygienist is that the tuberculin test in cattle as in man is positive in animals which while they may harbor foci of the disease are not actively tuberculous, that is, the reaction may be given by cured cases. If we were to apply to man routine tuberculin tests it is certain that we should find many supposed and actually healthy individuals who would respond to the reaction. The term "Reactor" is therefore indiscriminatively applied by stock men to animals perhaps not actively or obviously tuberculous and yet which simply give the reaction. It is found, however, that when such stock, apparently otherwise sound, be housed and fed with perfectly healthy non-reactors the non-infected herd sooner or later become widely diseased for the sensitiveness of uninfected animals to tuberculosis is remarkable and apparently much greater than in man. The common practice of dairy men is to largely ignore this fact, to take the chance as part of the risks of the business, and to eliminate only such animals as are obviously sick. These usually form but a small percentage of the real reactor group and under such methods the disease can never be eliminated from the herd.

The problem then becomes very complex particularly from an economic standpoint. It is true that thorough pasteurization of milk will eliminate the possibility of transmitting tuberculous infection to man. I do not propose to enter into the discussion of this problem at this time but to especially point out that reactors in any herd eventually cause the more or less complete infection of that group.

The experiments conducted at Woodcrest, previously reported,²

² Trans. Soc. Exp. Med. and Biol., 1914, vol. xi, No. 2, p. 50.

have apparently furnished a solution for this problem though it must be admitted a very expensive one indeed for the breeder of moderate capital since it practically necessitates separate and distinct establishments and personnel, and enough capital to permit a more or less idle and largely non-productive group of animals.

To me personally the fact of greatest interest has been that the inbreeding of tuberculous animals has in no way impaired the type or desirability of the offspring. It has been conclusively shown that the calves are very rarely, if ever, infected before or at birth. That the slightest carelessness in exposure of the newborn calves to infection leads to certain disaster is illustrated by ten recent infections at Woodcrest through the negligence of one workman in not minutely following out the instructions laid down. Tuberculous animals of desirable types may therefore be freely used for breeding purposes provided that the calves are not allowed to come in contact with the infected parents. The economic as well as the biological importance of this apparent fact is obvious.

To establish the fact that reactors may furnish and perpetuate most desirable traits as to type, fertility, milk, and cream production, and to therefore contravert the suggestion that such infected animals should be utterly destroyed, notes of the following group of animals are presented, taken by permission of Mr. Dimick from the records of Woodcrest Farm.

Pietje 22d, No. 70884. The foundation dam of this strain was imported from Holland by the Woodcrest Farm. She was supposedly of the highest type representing the Holstein-Friesian breed and her pedigree shows descent from the finest animals of this stock. It has not been possible to ascertain whether or not she was derived from tuberculous parentage but early tests at the Woodcrest Farm showed her to be a "reactor" although apparently in perfect health. She died of generalized tuberculosis at the age of fourteen years, four months. She is credited with four calves born in Holland and seven in this country. She made the following remarkable record:

Butter, seven-day test	31.62 pounds
Milk, seven-day test	673.90 "
Butter, thirty-days test	128.37 "
Milk, thirty-days test	2786.40 "
Butter, six-months test	566.60 "

This last item is stated to be the world's record for butter production for this time. During this same period she produced 13,673.90 pounds of milk. While at the Woodcrest Farm she gave birth to an annual calf with records as follows:

(1) Woodcrest Pietje. A bull calf; a perfect and effectively fertile specimen, sold as a herd bull. This animal is not known to be tuberculous, although it is strongly probable that he is.

(2) Pietje 22d's Woodcrest Lad. This animal is a perfect specimen in every respect and has been retained at the head of the Bou-

tekou Farm as a stud animal. He is known to be tuberculous and is isolated with the tuberculous herd. A daughter of this animal has produced at the age of four years 35 pounds of butter in seven days. This is stated to be a world's record for this age.

(3) Pietje 22d's daughter. This animal at birth was a perfect specimen in every apparent respect, although she was found to be tuberculous in the second year of her age. Her record is as follows:

Butter, seven days	25.19 pounds
Milk, seven days	553.40 "
Butter, thirty days	104.29 "
Milk, thirty days	2202.22 "

She was fertile each year and her offspring have all been perfect specimens of their kind. She died in January last from a generalized tuberculosis one week after the delivery of her last and perfect calf. This animal has not yet been submitted to the tuberculin test but inasmuch as it was removed from the mother immediately after birth, from previous experience, it is assumed to be non-tuberculous. She was the dam of Woodcrest Jamaica Pietje; a bull calf, perfect in every respect and now the head of a valuable herd. This animal has proved to be normally fertile. A daughter in her second year has given a butter record for seven days of 16.07 pounds, and of milk for the same time of 350.30 pounds. Woodcrest Jamaica Pietje was removed from the dam at birth, isolated from the tuberculous herd, and is free from any disease. Also dam of Woodcrest Johanna Pietje: A perfect and fertile bull. He is free from tuberculosis as he was removed from the dam immediately after birth. Dam also of Woodcrest Pietje Pontiac: A perfect male specimen removed from the dam immediately after birth and consequently free from disease. This animal was sold while a calf for \$2000, and is the anticipated head of a valuable herd.

(4) Pietje 22d's second daughter. This animal has always been tuberculous having received the infection apparently from her dam shortly after birth, nonetheless she was in every way a perfect specimen and gave a record of butter production for seven days of 29.63 pounds; of milk in the same period 584.70 pounds. Butter thirty days, 117.24 pounds; butter for one year, 829.53 pounds. Milk for the same time, 19,722.90 pounds. This animal died apparently from a generalized tuberculosis in September, 1913. She had been fertile each year since her maturity and all her calves were normal specimens. Three of these offspring are recorded all perfect, typical, and fertile in every way.

(5) Pietje 22d's son. This animal is a perfect specimen, although found to be tuberculous at the age of one year. He is at the head of a herd, serving about 100 animals yearly; is very fertile and typical of the breed in every way. His first five daughters at two years of age average over 18 pounds of butter in seven days each and over 4 per cent. of fat.

(6) Pietje 22d's third daughter. Found to be tuberculous at three years of age; after having successfully passed two prior tests. Her record shows butter production in seven days, 16.07 pounds; milk production seven days, 302.30 pounds. This animal is the dam of one heifer which has not yet freshened but which is a perfect specimen of her class.

(7) A bull calf, the last offspring of this remarkable cow, died of an infantile diarrhea in its very early youth, before it had been registered.

The male parentage in many if not most of these instances has been also tuberculous in all probability. The question of whether or not the offspring became tuberculous depends entirely upon exposure after birth. The point of greatest importance illustrated by this remarkable family is that no defects of a biological nature have been found in any of the offspring of this definitely tuberculous stem. All are perfect specimens. There has been no reduction in fertility, and judging from the milk and butter records no diminution in butter or milk production, and as stated, several world's records have been attained by these animals.

This family is apparently fairly illustrative of others of like nature, and in so far as the observations go it seems definitely demonstrated that parental tuberculosis in the cow causes no defects to be apparent in the offspring even though the calf be born in the almost terminal stages of the disease in the dam.

This report is also intended to point out that the term "reactor" as used by stock men often means what in human medicine would be classed as healed tuberculosis. It seems to show that definitely tuberculous animals may be safely utilized for breeding purposes and that they may be crossed and inbred with entire disregard of the factor of tuberculosis and purely for the purpose of improving or maintaining type. Most important of all, the fact stands out that although it may not be wise to utilize the unpasteurized milk of reactors for human consumption nor yet for the feeding of calves or other animals, yet reactors may be successfully and safely used as brood stock and thus cease to be an economic waste.

NOTES ON THE EXAMINATION OF THE URINE FOR TUBERCLE BACILLI.

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THE well-known difficulties attending the accurate diagnosis of tuberculosis of the kidney and bladder make it important to use every possible device to increase the probability of finding the

tubercle bacillus when it is present, as well as of eliminating all sources of error. In a patient recently seen I was able to make the diagnosis of vesical tuberculosis by finding the organism which had been previously overlooked. This patient was a woman who for two years had suffered from the usual distress attending bladder irritation. In spite of the persistence and severity of the symptoms, thorough search for tubercle bacilli had not been made. The urine was indeed so clear that one was justified in assuming no severe lesion of the bladder to be present; and the patient had, as a matter of fact, been regarded as a neurasthenic, a diagnosis which was justified by her temperament. Cystoscopy, however, showed a definite linear ulcer in the vault of the bladder above the right ureter, well away from the trigone. The rest of the bladder showed no definite changes, though there was slight dilatation of the vessels throughout. The ureteral orifices were normal.

It seemed to me necessary to obtain material from the surface of this ulcer if the diagnosis were to be made. I therefore distended the bladder with water to the point of discomfort—indeed, sufficiently to cause a slight hemorrhage—and saved the washings. In the washings, after centrifugation, several clumps of tubercle bacilli were found; these had doubtless been washed off the surface of the ulcer. The ureters were both catheterized and the urine injected into guinea-pigs, with negative results. The patient is having the usual up-and-down career of vesical tuberculosis, and is thus far to be regarded as a case of primary bladder tuberculosis without demonstrable kidney lesion.

The important point brought out by the case is the fact that in vesical tuberculosis, if the ulcer is on the vault of the bladder, where it is seldom or never reached by the small amounts of urine present there at any one time, tubercle bacilli may quite readily be absent from the urine, or at least not present in great number. In such cases, therefore, and indeed in all cases of vesical tuberculosis, one should add to the catheterized urine to be examined for the organisms, washings from the bladder surface. In obtaining these washings it is, I think, advisable to allow fluid to flow in until the bladder is distinctly distended, so as to obtain material from its whole surface. I have been impressed with the frequency with which tubercle bacilli may be found in genito-urinary tuberculosis if careful search is made. Indeed, I have thus far seen only one case, with negative urinary examination, in which the guinea-pig inoculations were positive. In this patient the specimen was sent from a distance by the family physician and only one examination was therefore possible. In this urine the organisms were not found, though guinea-pig inoculations were positive.

THE PRESENCE OF TUBERCLE BACILLI IN THE URINE IN GENERAL MILIARY TUBERCULOSIS. Some years ago I endeavored to determine whether or not the smegma bacillus was present in the bladder.

It had previously been shown that it was not present in the posterior urethra. The bladder urine was studied by aspirating it under aseptic conditions in routine cases at postmortem in the Johns Hopkins Hospital. In the first case thus studied I was surprised to find in the urine, after centrifugation and staining, many large clumps of organisms deeply stained with the carbol-fuchsin. These were at first interpreted as smegma bacilli, but on looking up the pathological report of the case it was found to be one of advanced general miliary tuberculosis, with lesions in the kidney, ureters, and bladder. This patient had gone to autopsy with a doubtful diagnosis. I then looked over the histories of the cases of general miliary tuberculosis at the Johns Hopkins Hospital and found that in nearly every instance in which the urine was examined for the organisms they were found present; but that in the majority of instances no urinary examination for tubercle bacilli had been made, although the sputum had been examined with great care. The point brought out by these observations is that in suspected general miliary tuberculosis (a disease, as is well-known, readily confused with typhoid fever and other febrile conditions) the urine should be examined for tubercle bacilli, for the value of urinary examination in these cases is far greater than that of sputum examination.

ALBUMIN IN THE SPUTUM IN TUBERCULOSIS: ITS VALUE IN DIAGNOSIS AND PROGNOSIS.¹

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DOUBTLESS we shall always place our chief dependence upon physical examination for the recognition of pulmonary tuberculosis; however, there are times when even the keenest examiner would like to have corroboration of the suspicions which have been aroused by his findings on physical examination. Of the numerous tests applied to such suspects, in the hope or expectation of confirmation of the diagnosis of tuberculosis, such as the various tuberculin reactions (the cutaneous of von Pirquet, the subcutaneous, the percutaneous of Moro, and others; the intradermal of Mantoux and the ophthalmic of Calmette); the sero-agglutination of Arloing and Courmont; the precipitin test of Bonomé and Vincent and Combes; Wright's opsonic index; anaphylaxis (Marmorek); the cobra poison reaction; and finally the fixation test, all leave something wanting. Some, or rather most, of these require too elaborate

¹ Read before the North Carolina State Medical Association at the annual meeting at Raleigh, June 16, 1914.

laboratory facilities and too skilled workers to be at the command of the general practitioner, and others are of such dilicacy as to give positive results in febrile conditions other than tuberculosis; and all of them are open to the criticism that they fail to show whether the patient who reacts is suffering from active, latent, or healed tuberculosis. In an effort to find some simple means by which any physician can corroborate clinical suspicions or evidences of pulmonary tuberculosis the albumin reaction in the sputum has of late come into vogue, with the hope of furnishing conclusive evidence of active tuberculosis or by a negative finding excluding the possibility of tuberculosis. It was with the hope of determining for our own future guidance and dependence the exact value of this addition to our diagnostic and prognostic methods that we have undertaken the examination of the sputum in a certain number of cases with a survey of the available literature, the results of which we now present.

The first mention of albumin in the sputum was made by Biemer,² in 1855. The statement attracted no particular attention, though Wanner, in 1903, stated that all sputa contained albumin, liberated through decomposition. However, the attention of the profession was not focussed upon this matter until the report of Roger and Levy Valensi³ in 1909, who claimed that albumin was found almost constantly in the sputum in tuberculosis, but was not present in chronic bronchitis, maintaining, further, that two negative examinations of sputa for albumin excluded tuberculosis.

Naturally such statements, together with the simplicity of the test which puts it within the hands of all, at once elicited the interest of numerous observers who commenced examinations in the effort to corroborate or disprove these views. At present, however, though quite a few observers have presented the results of their studies on this subject, there is a striking lack of unanimity of interpretation of the results, particularly insofar as the test may be considered an addition to our diagnostic methods for the early recognition of tuberculosis.

The sputum for examination should be carefully collected and as little mixed with saliva as possible. Saliva contains variable amounts of protein which may react to the test for albumin, hence the sputum should be as nearly saliva-free as possible, being obtained from below the glottis. Blood in any amount and particles of food should be excluded, as they impair the accuracy of the observations. In our own tests the sputum has been collected in an open-mouthed bottle, mixed with an equal amount of tap water (though some prefer distilled water), mucin precipitated with a few drops of acetic acid, and the whole vigorously shaken and then allowed to stand. It is then filtered through a wet filter paper and the filtrate examined

² Die Lehre vom Auswurf, Würzburg, 1855.

³ Société Médicale des Hôpitaux, 1909, vol. xxviii.

by any of the ordinary tests for albumin; that is, heat, 10 per cent. potassium ferrocyanide, etc.

The question of the diagnostic and prognostic value of the reaction has divided observers into two or more classes, according to the results of their observations; opinions ranging from unqualified acceptance of the test as proof or disproof of tuberculosis to absolute disbelief in its value as a diagnostic means in tuberculosis. Brown and Ross,⁴ of the Adirondack Cottage Sanitarium, conclude from an examination of the sputa of 116 cases in various stages of the disease that all patients with bacilli of tuberculosis in the sputum give a positive albumin reaction; that the degree of the reaction is proportional to the stage of the disease; that the reaction may occur only during an exacerbation of the trouble; and that a positive reaction by itself is of little diagnostic value, and in no way parallels the tuberculin tests for the determination of tuberculosis. They found that one examination was very inconclusive and on several occasions found a positive reaction after several negative findings. The repeated negative findings in cases of acute miliary tuberculosis probably mean that there is no active pulmonary tuberculosis.

Biernachi⁵ says that a positive albumin reaction in the sputum has diagnostic worth only within limitations. An albumin content of more than 2 per cent. bespeaks a manifest character for the tuberculosis, a conclusion which we think will stand without fear of contradiction. An inflammatory or destructive process of lung tissue being excluded, we can, he thinks, diagnose tuberculosis upon the grounds of a positive albumin-sputum reaction.

Schmitz,⁶ after an examination of the sputa of 100 cases, finds that in most cases of incipient tuberculosis, albumin is found in varying amounts in even sparse sputum without the presence of bacilli, though in undoubted cases of tuberculosis, for example, fibrosing and proliferative forms, no albumin may be found in the sputum. The albumin reaction, he concludes, is not reliable for the early diagnosis, but bears a direct relation to the degree of the illness, being greater with the progress of the disease, and hence has perhaps a value in prognosis. It bears no relation to albuminuria. However, it is so simple and easy that it is a welcome addition to our diagnostic procedures.

Eiler Hempel-Jorgensen,⁷ after a series of tests (in tuberculous as well as other cases), found albumin in the sputum in ten cases of bronchitis with emphysema and asthma in varying amounts

⁴ The Albumin Reaction in the Sputum in Pulmonary Tuberculosis, Transactions of the Seventh Annual Meeting of the National Association for the Study and Prevention of Tuberculosis.

⁵ Ref. by Schmey, *Tuberkulose*, 1911, No. 11.

⁶ Die diagnostische Bedeutung der Eiweiss-reaktion im Sputum, *Med. Klinik*, 20 Juli, 1913.

⁷ Ueber die Eiweiss-reaktion im Sputum, *Beiträge zur Klinik der Tuberkulose*, vol. xxvi, No. 4.

from a trace to 1.8 per cent. (3 per cent. was found in another case of bronchial asthma with bronchitis and emphysema, followed for several years without seeing any tuberculous development), and in pulmonary gangrene and croupous pneumonia. He thinks that the amount of albumin found in the sputum depends upon which part of the sputum is used and on the mechanical handling of it, since he found that there was a definite increase up to a certain moment, depending upon the amount of sputum which the patient had. He concludes, therefore, that the reaction as a diagnostic measure in the first stage of tuberculosis is not dependable.

Gelderblom,⁸ in an examination of seventy-five cases, always found that a positive albumin content of the sputum meant a fresh process in the lungs, and concluded that the rise and fall of albumin in the sputum was an index to the progress of the disease. The presence of serum-albumin in the sputum seemed to confirm Aufrecht's theory of the blood-borne origin of tuberculosis. He raises the interesting question, Would the systematic use of the albuminometer predict a hemorrhage?

Schneider,⁹ says that Eiselt, Goodman, Fishberg and Fellerbaum, Ljubarsky, St. Acs-Nagy, and Luczinin claim that the albumin reaction in the sputum has no diagnostic significance, whereas Busnikara, Levy, Pershaw, Brunner, and Pindberg claim that it is a great aid to diagnosis. He examined the sputa of 90 cases in his series. Tuberculosis was positively diagnosed in 74 cases, 64 of which gave a positive albumin reaction in the sputum. There were 14 non-tuberculous cases, of which 8 gave a positive albumin reaction, and 2 cases, which were probably tuberculous, also had positive reactions. He divided his sputa into mucoid, mucopurulent, and purulent, and says that all pussy sputum contains albumin, the amount depending upon the pus content. He concludes that the reaction is not specific for tuberculosis, being found in 8 cases out of 14 known definitely not to be tuberculosis, and also being negative in more than 15 per cent. of cases known to be tuberculosis.

The analyses thus far reported by the writer are most discouraging, but the work of Treadgold and Ridge,¹⁰ in a measure, contradicts the adverse reports above given. They report the results of their examinations of the sputa of 2164 cases, the largest number yet reported by any single authors. Of the first 2000 cases, 615 showed bacilli in their sputum, and in the entire series albumin was positive in 96 per cent. In the non-tuberculous cases examined albumin was found present in 32 per cent. and negative in 68 per cent. In the last 164 cases reported by them separately by reason of the greater

⁸ Deutsch. med. Woch., vol. xxxix, No. 41.

⁹ Die diag. Bedeutung des Nachweiss vom Eiweiss im Sputum, Lungenkranker, Zentralblatt f. innere Med., October 1913, No. 41.

¹⁰ The Albumin Reaction in Sputum; its Significance and Causation, Lancet, August, 1913, pp. 382 et seq.

carefulness with which the observations were made, albumin was found to be positive in 98.9 per cent. of definite tuberculosis and negative in only 1.1 per cent. Neither bacilli nor albumin were found in 25 cases of bronchitis, 2 of bronchiectasis, 1 of laryngitis, and in 14 cases clinically tuberculosis, but not active; from which observations they conclude that all active tuberculosis patients show albumin in the sputum; that the positive albumin finding in doubtful early tuberculosis supports the diagnosis; that three successive negative albumin findings with no bacilli in the sputum are strong evidence against tuberculosis; and that the test has considerable value in chronic tuberculosis and emphysema as evidence of activity when found to be positive. They have further made cytological examinations of these later specimens, and invariably found when the albumin reaction was positive there was a relative increase in the number of alveolar cells, which confirms the belief of all observers that the presence of albumin in the sputum is always associated with an alveolitis.

Ritter¹¹ found the reaction positive in 100 per cent. of cases with bacilli and in 78 cases out of 108 suspects. Though all bacillary cases gave a positive albumin reaction the amount of the albumin was not proportionate to the number of bacilli found, just as the number of bacilli found is not always a safe index to the severity or extent of the lesion. Ritter's enthusiastic support of the test as a diagnostic measure is shown by the sub-title of his article, which reads, "Its great value as a reliable and positive diagnostic laboratory method for differentiating pulmonary tuberculosis from other pulmonary diseases."

Our cases have numbered only 20 and are too few in number from which to reach conclusions, hence this survey of the literature on the subject. They were for the most part frankly tuberculous cases and the results were not significant. We found that wherever there was an exudative process in the lungs albumin was found, the amount bearing apparently some ratio to the degree of activity though no quantitative analyses were done, and hence we cannot speak definitely on the point. In one suspicious case a sputum which showed no bacilli gave a distinct albumin reaction, the diagnosis of tuberculosis never being confirmed, though there is every indication that the patient has had a massive fibrosing pleurisy which at the present gives no evidences of activity. Just why this patient should have a positive albumin reaction in his sputum when there is no discernible evidence of alveolar trouble we are not prepared to say.

While no attempt has been made in the cases reported thus far to separate the forms of protein, it may be stated that an excess of globulin is favorable while an excess of serum-albumin is usually

¹¹ The Albumin Analysis of the Sputum, *Med. Rec.*, April 26, 1913

associated with fever, emaciation, night sweats, and an advancing process (Smolizanski). We have been able to collect from the literature the results of the analyses of 3951 cases in all stages (not including our own), in which there was a positive albumin reaction in the sputum in 3778, or 95.6 per cent. These cases were all definitely known at the time or later proved to be tuberculosis, so that the conclusion is inevitably forced upon us that the large majority of all cases of tuberculosis show a positive albumin reaction in the sputum. It is, of course, known that albumin is found in the sputum of all pneumonias, and quite frequently in caseous bronchopneumonias and cardiorenal diseases; but difficulty in differential diagnosis here from tuberculosis does not usually persist for any length of time.

From our own limited experience with the test, as well as a review of the literature on the subject, we may conclude:

1. All cases of pulmonary tuberculosis showing bacilli give a positive albumin reaction in the sputum.

2. Frequently albumin will be found in the sputum in incipient tuberculosis before bacilli are present, but its presence is variable and it cannot be relied upon as a definite means of diagnosis in incipient cases.

3. The amount of the albumin present in the sputum in tuberculosis depends upon the extent of the exudative or destructive process in the lungs, is always associated with an alveolitis, and may be an index of the activity of the process, the heavier the albumin content the more activity present.

4. Certain (fibrosing or proliferating) forms of definite tuberculosis fail to show an albumin reaction in the sputum. Cases cured for two years or more will not show it.

5. When physical signs and the tuberculin reaction fail to show activity the presence of albumin in the sputum may do so.

6. As a diagnostic means its value is limited and relative and the result of a single examination misleading. It perhaps has greater value prognostically, as above shown.

7. The test deserves wider use until its exact value has been determined.

A PERSONALITY STUDY OF THE EPILEPTIC CONSTITUTION.¹

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VARIOUS mental tests in epilepsy, such as the Simon-Binet and others, have shown that there are two fairly distinguishable types

¹ Read before the American Psychopathological Association, Albany, May 6, 1914.

of mental state in this nervous disorder: (1) the 'general nervous constitution, the mental *anlage*, antedating or independent of the dementing disorder of epilepsy itself, and (2) that more or less considered dependent upon the disease as a deteriorating malady. From the different schematic tests alluded to above it is inferred that the mental equipment of those contracting epilepsy in later life presents an intellectuality not very dissimilar to that seen in certain mild types of mental defectiveness as seen in the moron. Be this as it may, a matter of equal moment in such inquiry is to determine so far as possible the character and personality of such individuals who are potential epileptics independent of any mere intellectual test. An investigation of the manner, conduct, and behavior of such persons is of the utmost importance to enable us to prevent the sequential epilepsy in such individuals if possible. In a review of the more recent literature upon the epileptic constitution, one is impressed with the fact that there is much evidence to support the contention that a fairly well-defined constellation of personal characteristics shown in the epileptic constitution applies to many of the relatives of those actually epileptic. Although such relatives may not have seizures or actual convulsions, and are not classed as real sufferers from this disorder, they may still be ranked as potential epileptics. As a matter of personal belief, not fortified at this moment by actual statistics, we believe we rarely see an epileptic patient in whom we may not demonstrate in the family history certain types of neuropathic makeup which to me are different from that ordinarily encountered in the hereditariness of other neuroses or psychoses. We are aware that a reverse argument might generate the inquiry: How often does one encounter this degenerative epileptic constitution in a family stock in which no frankly convulsive epilepsy actually occurs? To this inquiry we should reply that we believe it occurs very frequently. It is precisely in such degenerative soil one often encounters the affect epilepsies of Bratz' type—the psychogenic convulsions which are really, in most instances, the incompletely evolved genuine epileptic. Here, too, one encounters certain types of fulminant psychoses, such as the acute hallucinoses, the constitutional psychopathic inferiors, in which latter class, under the influence of alcohol or some keen emotional stress, various acts of destructive violence occur. Many another mental disorder has its outcroppings from such family degeneracy. The very epileptic manifestations in some neuroses and psychoses have led not a few reporters to greatly extend the application of epileptoid states in the psychoses. Further analysis of the wisdom or the reverse of this position would carry us too far afield at this time. Instead we intend to give the result of an analysis of the personality makeup of a small but select material of epilepsy which we shall make into a composite of the epileptic constitution. To each individual in the series, Hoch's

method of detailing the makeup of the adolescent insanities has been applied. We believe the results of such examinations carefully controlled, as they have been, and especially when the material is selected from the better class of epileptics, will prove worthy of report. The sources of information to the subject matter have been taken from one or the other parent, and the same has been frequently controlled by other collateral sources in and out of the family to make the information as accurate as possible. It is interesting to note that we have recently applied the personality study to two or three of our arrested cases of epilepsy who have been free from seizures for several years, and we have found that the makeup of the epileptic constitution which remains in such individuals is not dissimilar to that in the cases incorporated in this report who are still epileptic. From this and other data it is obvious that so-called cures do not include an essential alteration of the personality to which fruitless task so many epileptologists direct their correctional treatment.

The foregoing fact is of more than academic interest, inasmuch as if the same holds true in a large material one must believe that the appearance of actual epileptic seizures in such cases are really epiphenomena, and that which really should concern us most in recovering such epileptic individuals should be the eradication of the seizure manifestations of the epileptic state. While such a view would seem to narrow the problem of therapy in one direction it extends it in another, making us keenly aware of the great importance of a better knowledge of organic chemistry of the body and the various mental factors that deteriorate neuropathic individuals. As a preliminary to the small study here set forth we may say that the Binet scale shows no intellectual deficit in any of the epileptics under study. All who show congenital defects have been excluded from the examination.

Before entering upon a detailed analysis of the cases we may say that the personal traits of these potential epileptics were made to include all those evidenced from earliest infancy up to approximately sixteen or eighteen years of age or until their epilepsy began. None of the cases embraced in the study had attacks oftener than once or twice a month, an average grade severity of epilepsy. Five boys and five girls were included in the material studied. No personal characteristic that might be considered to be even slightly tainted by the oncoming epilepsy was allowed a place in the examination material.

With one exception the whole group learned easily, although the greater number had to study hard to keep in their grade. The standing in school was fair in all and above the average of their class in the majority, and in two the daily standing in the class work was sufficiently good to excuse them from final examinations. None missed a grade in their entire school life. It is interesting

to note the school subject in which half of this epileptic group was specially proficient was literature and an equal number were deficient in the same. It is also interesting to find that the two subjects of literature and mathematics were combined in being good and bad respectively in the same individual in five each. In but one was the education not up to the opportunities of the pupil, showing a diligence and perseverance not often reckoned in the educational makeup of the epileptic. Attention and power of concentration were uniformly good in all with but one exception. They were all considered capable in any of the duties they were called upon to perform. They also showed good common sense. The material was equally divided between those individuals who were quick and impulsive in their judgments and the reverse. With one exception they all planned their work and play with good foresight, and but one was impractical of mind and handled tools poorly, which goes to show in a small way that many potential epileptics are probably free from the defect of motor power and control so noticeable when the disease is well advanced. Many of this number, even though their disease has now existed for several years, make good designs and do excellent wood-carving and other handicrafts of a very superior order. They all were lively in work and play and never lazy and sluggish, which again is in marked contrast to this characteristic seen in those presenting the advanced diseases. None showed much imagination in play or work. For the most part these adolescents were rather silent and talked little even though often urged to do so. Without exception they were all energetic, and the greater number were overactive in work and play. The expenditure of their energies was for the most part desultory and not sensibly expended. This fact must, however, be taken with due reservation, as so-called adolescent normals vary so much in this regard, especially when viewed by adult eyes from above.

They were at all times self-reliant, and none ever showed any tendency to be self-depreciatory or show feelings of inferiority. As might be expected from the foregoing, none showed any dependence on others for comfort or for forming their opinions. They all were ranked either as openly possessing an egotistical makeup or the same was thinly disguised and easily provoked to the surface. This trait, of course, was most marked in the boys, just as the girls showed marked pride and vanity in manner and conduct. The majority of all were rather honest with themselves but were quite keen in emphasizing dislikes for shams in others, although the greater number were markedly genuine with themselves. Also most of them were little inclined to blame others for their own faults. Without exception the potential epileptic seems very little inclined to make much of his aches and pains, and not a few instances were shown where there was marked insensibility to ordinary painful injuries. The majority were not given to self-pity.

As a rule these boys and girls were socially inclined, but made little progress in such characteristics because the majority possessed so little ability to subordinate their own individuality to the common social demands, therefore their friendships were for the most part superficial. Friends were often easily made, but were as readily dropped or changed. None seemed to prefer to be alone when left to their own inclinations. The major portion of the subjects took reprimands illy and usually sulked a good deal under such discipline. All the boys were shy and bashful with strangers, while the girls for the most part were not. As might be expected from the foregoing egotistic characteristics the greater number of these children did not play naturally and freely with others; they had always to be leader, and the presence of such a disconcerting characteristic even normal children will not long endure if there be other resources of play. The greater number of both boys and girls were inclined to selfishness, yet were all fairly sympathetic and kind-hearted, but not altruistic. The latter fact is not so disharmonious, as it is often encountered in the normal adolescent character. They were pernicious and not generous for the most part. The majority were moderately tactful and not offensive or quarrelsome, again in marked contrast to the character of the frank epileptic of adult life.

On the whole these potential epileptics were easy to get along with and could cooperate with others fairly well for a short time. Singularly enough, while they all wanted their own way, they were not specially disobedient in early childhood or in early adolescence, in marked contrast to their wayward disposition in early adult life. On the whole both boys and girls were inclined to be of a rather suspicious and resentful nature, but were not easily offended and saw no slights where none were intended. The majority were not of a jealous or envious disposition, and thought the world treated them fairly well, and also felt satisfied with their environment. They also easily adapted themselves to new environments. There was a rather marked shallowness and superficiality of the inner life, as conveyed to others, and none were specially open and frank in discussing the same with anyone. They were, as a rule, not demonstrative. Without exception they were thought to be conscientious and with a fair feeling of responsibility. There were no blocking by scruples, no commitment to routine, nor finicky demands for special precision and order. They were all inclined to want to lead and showed great demands for self-assertion. On the whole they were brave and courageous as children, and not in the least imitative or suggestible. They took things as they were and never day-dreamed or built air castles. They were also trustful, cheerful, and light-hearted children. As a rule they were of an even mood, optimistic, hopeful, and of apparently normal reaction to good news, success, etc. There were no worries, despondencies, but real bereavements were almost always sharply reacted to, although

in a transitory manner. The craving for sympathy and petting was little noted. Evidences of anxiety and forebodings were not encountered in any of the individuals of the study. Singularly enough the majority of the boys and girls were not especially irritable or quick-tempered, and such reactions when present were short-lived. None apparently showed childish tantrums, which is rather remarkable in the neuropathic makeup. The majority were neither touchy nor sensitive, yet were not phlegmatic or indifferent to acts and remarks of others.

There was a strong resemblance in physical and temperamental makeup to one or the other member of the family in all cases, and it usually leaned toward the side with the strongest hereditary neuropathy. There was always apparent a rather marked antagonism to one or the other parent, which was as frequently directed against the one parent whom the child resembled as not. The girls for the most part inclined to be tomboys in manner and conduct, while the boys were not effeminate in manner and behavior. But one of the ten was specially attracted to the opposite sex, and practically no love affairs were unearthed by most energetic inquiry. None were ranked as sentimental even when adult life was reached. All but one were kind to animals.

None showed special interest in a particular kind of work nor got much satisfaction out of any special occupation. None were specially ambitious children. All were interested in sports, at which they usually excelled as well as the average normal child. They seemed to develop no hobbies or fads with the exception of one, who was very fond of and greatly excelled in tennis. As a rule they one and all took little interest in the news of the day and rarely made any genuine effort to understand the real processes of society at large. None showed interest in religious affairs even of a superficial character, and none were superstitious or interested in any form of religious gropings after the occult, etc. All the physical habits appeared to be normal. Sleep appeared normal in character and amount. But one occasionally had a few attacks of nightmare as a child of eight.

In taking the personality histories of epileptics, one is impressed with the great difficulty of getting at the basic facts in the patient's reaction to specific stimuli either from the patient or from the parents. We have undertaken to correct and supply certain data in the different cases where we have known the specific reactions to be diametrically opposed to the data given by the patients and relatives. However, we have not done this extensively in any one case. It must be remembered the majority of the cases have been under our detailed observation and supervision for a period of one to three years, and we have grown to know them very well; their reactions to various stimuli from day to day have been a matter of detailed record in each case. We suppose, too, our views on the

makeup of the epileptic constitution in a general way are not a little fashioned from the daily contact and experience with epileptics covering a period of several years' residence at the Craig Colony for Epileptics, although, of course, we made no such careful or detailed study of their peculiar constitution as attempted here. One may say with certain reservation that in the majority of youthful epileptics there does exist a fairly definite personality makeup differing widely from that seen in even the highest grade of feeble-mindedness, and, while in many instances one obtains no distinctive reactions to many of the temperamental traits in the main headings of the study, and even in a still greater number the reactions may be superficial or indecisive, there are categories which stand out in marked contrast to these other colorless parts of the study. It is worth while to briefly recapitulate these definite reactions in their order. As previously stated, in intellectual traits, the capacity for acquiring knowledge, and in the formation of judgment, our cases showed no essential departure from the normal; on the contrary, the majority ranked even higher than the mental development of the average adolescent of their age. The point, however, loses some of its force, inasmuch as those epileptic individuals were selected who presented no mental defect, in order that the traits commonly found in the congenitally feeble-minded that are more or less dependent upon intellectual defects might surely be excluded. In considering the traits relating essentially to the output of energy, we find a very definite reaction. As a class the individuals showed what might be called a supernormal output, which was rather constant and fairly productive of good developmental results. Probably the facts relating particularly to the subject's estimate of himself is one of the more striking characteristics of the epileptic constitution. Almost without exception this reaction impresses one as supernormal to a marked degree, a fact which, however, is so well known as to have already become historic. A comment, however, of greater moment, which is so obvious to even the casual observer, is the poorly repressed or inhibited egotistic tendency; even when it is held in check it is so thinly disguised as to be easily detected. Perhaps a warning note, however, should be sounded here, that one may easily go astray in this part of the personality study, inasmuch as the reaction is a purely quantitative one that may vary within wide limits without indicating much as a pathological character defect. Here as elsewhere specific examples of the different reactions were always obtained before a crude statement of the negative or positive character of the fact were recorded. This one principle alone, while essential to the analysis, makes personality studies very time-consuming. Many cases, even in experienced hands, require hours of painstaking labor. We believe it may be laid down as a fact that the fabric of the character formation of the epileptic constitution must be found

to hang together well and to blend smoothly in its color traits before one may rest content that the analysis is complete. This fact is essentially true, however inconsistent this principle may be in a personality study of the psychoneuroses and the frank insanities. The epileptic personality, we should say, is, on the whole, a consistent one.

The imperfect adaptations of the epileptic toward the environment is what one might expect from the foregoing statement regarding his estimate of himself. His keen individualistic attitude will become the more striking in future years when the progress of civilization requires greater and greater social and commercial coöperation. The epileptic is not naturally a gregarious individual, in sharp contrast to the feeble-minded youth. This trait in the epileptic character becomes the more noticeable as one studies the specific reactions of his adaptations in a less obvious way. Again, the very consistent compactness of the personality of the epileptic makes him an ideal of frankness. In many instances his not laying his real self bare to others may seem to presage a certain profundity of mind and character, but it really will be found that in the majority of instances the underlying content is superficial in makeup and of a relatively simple child pattern. This fact alone, we believe, renders him much less capable of the harm in the extremes of love and hate that he might otherwise exhibit. In our study one is rather impressed with the potential epileptic's diminished reaction to such traits of the useful qualities of inhibitions, such as conscientious scruples and doubts, and the demands for truth and justice. Such traits of character, inhibitions on the whole, seem to float over his head without perturbing his mind, which is only too often concerned with the lower strata of animal passions. There is none of the blocking of doubts of the obsessive neurotic in his makeup. The relatively high intellectual quality demanded in the compulsive neurotic may account for the epileptic being outclassed here. With the inhibitions reduced, and with an overemphasized estimation of his own ability, one readily understands with what conflicts the epileptic character meets when one studies his efforts to shape circumstances and situations to square with his desires. He is a born leader if self-assertiveness were the only requirement, and an almost infinite number of social and business failures have to be encountered to prove to him his defect. These wrecks only too frequently embitter him in later life and make him often an unpleasant companion or family associate.

On the whole the potential epileptic is not given to productive imagination, although this may not be an invariable rule, as one of our patients, not included in this study, is one of the most highly gifted, productive, and practical inventors of our day. He is, however, a rare exception in our experience. History has clasped the few epileptics of highly productive imagination to its pages for daily exploitation.

Contrary to the usually accepted criterion the mood of the epileptic constitution is singularly not much perturbed. Its disturbance is characterized largely by a certain shallowness and superficiality. Much of the intensive variation probably heretofore laid down in books is chargeable to the convulsive part of the later developing disorder and its well-known exhaustive and deteriorating effects. Here and there one sees outcroppings of family types of irritability and pathological sensitiveness in the makeup, but, on the whole, the personality is singularly free from the reactions of "moodiness" ascribed in the past to the epileptic character. Also, one finds that forebodings and anxiety play little part in the characteristics of the adolescent personality of the epileptic. When one capitulates the instinctive demands, especially those traits which are more or less clearly related to the sexual instincts, one is impressed again with the apparent shallowness of the reactions encountered. Friendship is a rather perfunctory characteristic. No doubt the egotistic traits prevent much of the free range of the outward expressions of affections. Friends come and go with the epileptic with little exhibition of heartache or break.

The parental antagonism toward one or the other parent, or both, is often marked. The future psycho-analytic study of this one factor and its aberrant sexual significance is of paramount importance in understanding the epileptic behavior and conduct. Psycho-analysis undoubtedly will reveal much for the homosexuality concept in parental fixations. To many this will seem the crux of this personality study of the epileptic character. We are disposed to agree with them. Still further their attitude toward the opposite sex is singularly significant. It is most often absent in its higher love attributes and most frequently evolves little beyond the grossest sexual satisfaction in many, and in others it plays little role in the character, at least in adolescence. To what degree the sequential epileptic paroxysms and the nervous and mental deterioration engendered thereby make for a breaking down of sexual control we have yet to learn. The mental deterioration in epileptics probably plays no small part in loosening many a buried and poorly repressed sexual desire of earliest life. No doubt the very paroxysmal character of the disease and its frequent reductions in every-day consciousness permit the epileptic to serve as an almost ideal individual for a study of the complexes of the unconscious activities. It will probably not be very long before we shall be obliged to rewrite the whole of our present-day knowledge of the mental states in epilepsy, and this will be done largely from the psycho-analytic studies of this experimental disease of disordered consciousness.

The certain sexual demands in the preparoxysmal stage are difficult of analysis in even small material, but the general impression one gains without a specific analysis is that they are usually intense. However, the teeming conflicts in sexual matters one sees

most frequently in the psychoneurotics are not so thinly masked in the epileptic makeup. The whole situation is grosser, deeper, fundamental, and more a matter of fact.

The lack of general interests, continuous and persistent, are noteworthy in epileptic adolescence, even when the extra variability and of so-called normals are taken into account. Singularly enough the religious promptings and allied gropings after the meaning and end of life are conspicuous for their absence. No doubt here too the after-development of the disabling and all too frequently hopeless disorder has much to do with the religiosity, real and false, of the frankly established epileptic type of character. It certainly forms little of the life interest of the preëpileptic stage of our study.

In conclusion it is interesting to note that this study is of more than academic interest in outlining the makeup of the epileptic constitution, inasmuch as the manifestations of the epileptic character as laid down in the text-books are in greater part due to the development and consequence of the disease of epilepsy itself. This is the more understandable when one bears in mind that the epileptic character is due in part only to the deteriorating effects of frequent seizures in themselves and also to a lack of opportunity of the epileptic in coming into ordinary every-day association with his fellows, and the consequences of being thrown back upon his own limited resources in a social way. This not a little indicates the importance of creating an artificial environment for the epileptic in order that he may correspond with his surroundings in a more or less simple and natural manner. Since paying particular attention to the character formation of childhood in epileptics we have been struck with the frequency in which one encounters children who afterward become epileptic in whom there are no marks or signs of the epileptic constitution. In such instances one is fairly certain that we deal with a sequential epilepsy in which an infectious or irritative agent acts more as an exciting factor, and in such one is impressed with the fact that those who have considered the disease as an infectious or postmeningitic disorder have more than a little evidence to substantiate their views.

REVIEWS

DISEASES OF THE SKIN, INCLUDING THE ACUTE ERUPTIVE FEVERS.

By FRANK CROZER KNOWLES, M.D., Instructor in Dermatology in the University of Pennsylvania; Clinical Professor of Dermatology, Women's Medical College of Pennsylvania; Fellow of the College of Physicians of Philadelphia, etc. Pp. 546; 199 engravings and 14 plates. Philadelphia and New York: Lea & Febiger, 1914.

IN this new manual of diseases of the skin, which the author states is intended for the student and practitioner rather than the dermatologist, moot points and matters of theory, very properly find but little place. In the description of the various diseases of the skin, while no necessary detail is omitted, all unnecessary elaboration is avoided. Special attention is given to matters of diagnosis and treatment, the author relying in the latter largely upon his own experience.

While the author is very conservative, in the expression of his own opinion perhaps too much so, he apparently has very decided convictions about the preponderating role played by external causes in the production of that very common and often distressing affection, eczema. In his experience fully 25 per cent. of all cases are of external origin; and one is, therefore, not surprised to find him declaring that external treatment is of paramount importance. The dietetic treatment of that usually obstinate disease, psoriasis, which has recently experienced a kind of mild rejuvenescence in some quarters, has failed to produce appreciable results in his hands.

In the endeavor to cover the whole subject of diseases of the skin a number of very rare and but little understood affections, such as trophedema, goundou, gayle, have been included which might very well, in our opinion, have been omitted in a manual intended for the student, and the space given to more important diseases.

A distinguishing feature of the book is the large number of illustrations, most of them black and white reproductions of photographs from the author's own collection, which add decidedly to its usefulness.

We are sure the book will be found useful by the student and practitioner, for whom it has been prepared. M. B. H.

DISEASES OF THE RECTUM AND COLON. By JEROME M. LYNCH, Professor of Rectal and Intestinal Surgery, New York Polyclinic. Pp. 583; 228 engravings and 9 colored plates. Philadelphia and New York: Lea & Febiger, 1914.

PROCTOLOGY as a specialty is young and is largely in the making. That it will obtain a recognized place among the other special branches of surgery is very likely, although it can hardly be said to have done so as yet. The field is a very limited one, but, as in other specialties, those promoting it increase its boundaries by adding work on closely related portions of the body. Lynch includes the surgery of the colon with that of the rectum and anus, and while he does not intend this book to be "encyclopedic," he has "discussed the subject in very full detail." Much detail is obviously necessary to fill a book of this size on the few and already much studied affections of this limited portion of the body. Almost half of the book is given over to affections of the rectum and anus, the great mass of the material discussed affecting the region of the anus. The rest is devoted to affections of the colon, and here again the tendency is to justify the specialty by attention to detail.

But attention to detail makes for progress and justifies a book of this kind. Piles, pruritus, fissure, and fistula in ano offer a poor field for advance in methods of treatment; but these conditions are so common and so troublesome that any improvements in the details of the old and tried methods are welcome. The use of local anesthesia in rectal surgery, with its well-defined limitations, is an example in point. The author's method and small experience with extradural, sacral anesthesia is also of interest. At times a little more detail would be an advantage. For example, in discussing the surgical treatment of fissure in ano, one of the reasons given for opposing divulsion is that it requires an anesthetic. Incision is considered the only logical treatment, but we are not told how this can be carried out without an anesthetic. It would seem important to tell how deep an incision is necessary to divide the sphincter sufficiently to place this muscle at rest.

That the experience of men doing much work in this line shows that a relatively small number of fistulae in ano are of tuberculous origin, is interesting. It is also interesting to learn from the same reliable sources that recto-urethral fistulae are seen more frequently since perineal prostatectomy came into vogue. Of special value are the chapters on pruritus ani, cryptitis, and papillitis, and on constipation. The general practitioner and general surgeon will find that the best and most recent contributions in this branch of surgery are presented in this volume in a clear and comprehensive manner.

T. T. T.

RADIUM AND RADIOTHERAPY. RADIUM, THORIUM, AND OTHER RADIO-ACTIVE ELEMENTS IN MEDICINE AND SURGERY. By WILLIAM S. NEWCOMET, M.D., Professor of Roentgenology and Radiology, Medical Department, Temple University; Physician to the American Oncologic Hospital, Philadelphia. Pp. 315; 72 illustrations. Philadelphia: Lea & Febiger, 1914.

THE author is recognized as one of the foremost workers of America in radium therapy. The apparent paucity of English, and especially American, literature upon the subject appears to have been a leading inducement for him to undertake the compilation of this book. Radiotherapy is a comparatively new field in this country except among relatively few workers, but its employment is increasing by leaps and bounds, and the magazines are being flooded with articles on treatment by the radio-active elements. Dr. Newcomet has essayed to bring before the medical profession at large a compilation that will give them a superficial knowledge of the physics and chemistry of radio-active substances and a general idea of their applications and what may be expected of them as therapeutic agents. The author has made selections from the reported experiences of others and has added his own. The book as a whole serves well to introduce the subject to the medical profession in a concise manner. For the beginner in radiotherapy it will serve as a reference book, but the necessarily limited details concerning treatment will not give it a place as a text-book. Seven chapters of the first part are devoted to the history of development, chemistry and physics of the radio-active elements, and another to the various applicators and methods of application. The second part deals with physiologic action, special therapeutic applications and technique, and gives the reader a general idea of what has been accomplished and what may be expected from radiotherapy. The final chapter deals with the treatment of untoward effects of the radio-active elements.

H. K. P.

A TEXT-BOOK OF GENERAL BACTERIOLOGY. By EDWIN O. JORDON, PH.D., Professor of Bacteriology in the University of Chicago and in Rush Medical College, Chicago. Fourth edition. Pp. 647; 178 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

To this new edition of the well-known text-book several additions have been made. These include Pappenheim's staining method, Churchman's studies on the effects of gentian violet media, an amplification of the section upon anaphylaxis, with a very brief presentation of Vaughan's views on the importance of parenteral

protein digestion, a section on streptococcus sore throat, one on the bacillus abortus of cattle, on Mallory's studies with bacillus pertussis and on Flexner's and Noguchi's studies of the microorganism of epidemic poliomyelitis. A chapter on filterable viruses has been added, and to this has been transferred several sections previously placed in the appendix, including those on smallpox, yellow fever, hydrophobia, typhus, and foot-and-mouth disease.

Additions have been made to the chapter devoted to the pathogenic protozoa, especially in dealing with the trypanosomes, the leishmania, and the piroplasmas.

The book is intended to give an introduction to the subject of bacteriology in its bearing not only upon medicine, but also upon household administration, agriculture, sanitation, and the arts and industries. The first quarter of the book is devoted to general considerations, such as the history and methods of bacteriology, the general biology of bacterial growth and activity, the relation of bacteria to disease and immunity, and anaphylaxis. The middle half is occupied with the detailed consideration of the known pathogenic organisms, their morphology, cultural characteristics, pathogenic properties, modes of transmission, and immunology. The last quarter of the book contains chapters on the filterable viruses, the bacteriology of certain arts and industries, such as tanning, tobacco-curing, vinegar-making, etc., the bacteriology of the air, soil, and water, and the bacterial diseases of plants. J. H. A.

DISEASES OF THE STOMACH AND THEIR RELATION TO OTHER DISEASES. By CHARLES G. STOCKTON, M.D., Professor of Medicine, Medical Department, University of Buffalo; Attending Physician, Buffalo General Hospital, etc. Pp. 728; 65 illustrations, 22 radiograms, and 5 plates. New York and London: D. Appleton & Co., 1914.

THE charm and the value of Dr. Stockton's new treatise lies in the delightful personal note that runs through its entire length. We can read and learn what the illustrious author does with his cases, how he handles the treatment, and upon what he bases his diagnoses. We are instructed at first hand, and, while other authorities have been drawn upon, we become directly acquainted with the knowledge of a master of his art. Dr. Stockton need not apologize for the personal note; it represents the greatest value of the book and the one that will make it deservedly popular.

The forepart of the book deals with the anatomy and physiology of the stomach, the examination of the patient, the gastric contents, the stomach-tube, radiography, and fluoroscopy. Then are

considered, in several chapters, the functional and organic diseases of the stomach, as well as chapters upon the most important symptoms of gastric disorders. Probably the most valuable chapter to the general practitioner is the one upon the stomach in relation to other diseases. This is a fairly complete exposition, but it might have been made even more complete and broader in scope.

In considering treatment, Dr. Stockton is not sufficiently specific in some places. For example, in the treatment of gastropotosis seven pages are devoted to gymnastic exercises while nothing definite is told about the really important adjuvants to this rational treatment. Diet is dealt with in the most general terms, a criticism which applies to the dietetic consideration of nearly all the other disorders; belts and other abdominal supports are discussed with a word and no mention is made of hydrotherapeutic methods of treatment. One or two other minor suggestions may be made; the subject of auto-intoxication might well have received less attention, and several of the proprietary drugs suggested could have been omitted. These few criticisms are largely obscured by the general excellence of the book, the scientific accuracy of which is only surpassed by its splendid rationality and good common-sense. J. H. M., JR.

CLINICAL DIAGNOSIS AND URINALYSIS. By JAMES R. ARNEILL, A.B., M.D., Professor of Medicine and Clinical Medicine, University of Colorado. Second edition. Pp. 270; 84 illustrations. The Medical Epitome Series. Philadelphia and New York: Lea & Febiger, 1914.

It is remarkable, indeed, that Dr. Arneill, within the brief compass of an "epitome," has succeeded in presenting the wealth of material that this book contains. It is with interest that we note that when the customary tests of blood, stomach contents, feces, sputum, and urine are detailed, the author still finds room for tests, out of the beaten track of laboratory routine such as Wright's coagulation test, cryoscopy, and spinal fluid test for albumin and dextrose. The recent advances in serum diagnosis are likewise embodied, and include discussions of the Wassermann, Noguchi, butyric acid, and cobra venom tests.

The illustrations, which are numerous, well chosen, and enlightening, deserve mention, as do also the careful descriptions of such apparatus as the tests require.

As a ready and reliable means of giving the busy man a working grasp of what is worth while along the laboratory lines within his reach, the book can be heartily recommended. A. A. H.

THE JUNIOR NURSE. By CHARLOTTE A. BROWN, R.N., Instructor in the Boston City Hospital; late Superintendent of the Hartford Hospital Training School. Pp. 208; illustrated. Philadelphia and New York: Lea & Febiger, 1914.

THIS book was written for the purpose of supplying "the student nurse with a guide for the earlier months of her training." It considers fully, but with a clearness and simplicity which is delightful, the various cases and duties with which the junior nurse must be acquainted. In addition there is a chapter upon the qualifications of the nurse and a most pertinent one upon personal hygiene.

The material is well expressed and carefully considered. Exception, however, might be taken to the inclusion of some of the more complicated methods of diagnosis and treatment. Eliminating this possible objection, there remains such a clear exposition of what the nursing neophyte should know that it is difficult to imagine the book not having an immediate and hearty welcome.

J. H. M., JR.

PRACTICAL PEDIATRICS. By JAMES H. MCKEE, M.D., Professor of Pediatrics in Temple University, Philadelphia; Visiting Pediatrician to Philadelphia General Hospital, Garretson Hospital, and Samaritan Hospital, Philadelphia; and WILLIAM H. WELLS, M.D., Assistant Professor of Obstetrics, Jefferson Medical College. With an Appendix upon Development and its Anomalies. By JOHN MADISON TAYLOR, A.M., M.D. Associate Professor of Non-pharmaceutic Therapeutics, Temple University, Philadelphia. Pp. 1182; with two colored plates and 146 illustrations, including 238 figures. Philadelphia: P. Blakiston's Son & Co., 1914.

To use the authors' words, "they have endeavored to present succinctly much more than a treatise on disease as it appears in the young . . . not only the recognition and repair of abnormalities and disturbances, but also prevention in the widest sense of the word." In this we see the tendency of modern medical writings, and the authors' aim, it may be said, has lent a distinctly improved flavor to the taste of the average text-book. The study of the child, as contrasted with the study of the illness of the child, is given due emphasis. Within the large compass of the book, space is afforded for ample consideration of diseases, including those of the ear, nose, and skin, with a comprehensive discussion of diseases of the nervous system. The appendix forms an addition, novel in the treatment of the subject rather than in the subject matter itself. Some of it is couched in language which, it is to be feared, will hardly convey a clear conception of its meaning to those not versed

in psychological literature, while the practicability of the application of its teaching, at times, is questionable. With the views on instruction in hygiene of sex many will not agree. For example; "the sooner the child learns the truth about sex . . . by so much will one of the gravest perils be reduced to determinable proportions." It is to be feared that such practise will result in the fervent wish that the "proportions" had never been "determined." The chief criticism of the book, as a whole, lies in a tendency to polypharmacy in the treatment of some diseases, notably pulmonary tuberculosis, while the desirability of vigorous local treatment of the diphtheritic throat certainly is questionable. Sins of omission are few, but surely pylorospasm, gastroduodenitis in relation to jaundice, vaginitis, and the dietetic treatment of migraine and migrainous affections deserve more consideration than mere mention.

On the other hand, there is vastly more to praise than to blame. The book gives an excellent presentation of pediatrics; is full of practical suggestions resulting from the personal experience of the authors; profusely illustrated with well-selected and, in the main, original subjects; completely indexed, and last, but by no means least, admirably printed.

J. C. G.

THE LIFE AND LETTERS OF NATHAN SMITH, M.B., M.D. By EMILY A. SMITH. With an introduction. By WILLIAM H. WELCH, M.D., LL.D. Pp. 185; 25 illustrations. New Haven and London: Yale University Press and Oxford University Press, 1914.

NATHAN Smith was preëminent in the medical profession of New England in the quarter of a century following the Revolution. Especially was he active in connection with the medical schools which sprung up in that section during his lifetime. He actually initiated the Dartmouth Medical School, 1798; he held professorships at Yale, 1813 to 1829, and at Bowdoin, 1821 to 1823; and he was associated in the foundation of the medical school of the University of Vermont. This volume is a contribution by the Yale University Press to the celebration of the centennial anniversary of the opening of "The Medical Institution of Yale College." Mrs. Smith has not only brought together the essential published facts regarding Dr. Smith's life, but has made a substantial contribution to that literature by publishing for the first time his letters to his friend and pupil, Dr. George Cheyne Shattuck, of Boston. These letters cover a period of twenty-five years, and give a clear insight into the personal, family, and professional sides of his life. Dr. William H. Welch compares these letters to those of John Hunter to his former pupil, Jenner.

T. G. M.

A MANUAL OF INFANTILE PARALYSIS, WITH MODERN METHODS OF TREATMENT. By HENRY W. FRAUENTHAL, A.C., M.D., Surgeon and Physician-in-Chief, New York Hospital for Deformities and Joint Diseases, and JACOLYN VAN VLIET MANNING, M.D., Epidemiologist, Wisconsin, 1908. Epidemic Acute Poliomyelitis. Pp. 374; 128 illustrations. Philadelphia: F. A. Davis Co., 1914.

THE book is based chiefly on a compilation of statistics from various sources. The value of some of these can be questioned. For example, data furnished by general practitioners scattered throughout a state may possess some interest but can hardly be considered scientifically valuable. Apart from the variance due to the personal equation among a large number of observers, the difficulty in a correct interpretation of many of the clinical, and especially the neurological findings, in such a disease as poliomyelitis, renders such statistics of little real worth. On the other hand many quotations and excerpts are from trustworthy sources, so that the book contains a mixture of what may be called wheat with the chaff of medical opinions.

J. C. G.

THE MEDICAL DISEASES OF CHILDREN. By T. R. C. WHIPHAM, M.A., M.D. (Oxon.), M.R.C.F., Physician to the Evelina Hospital for Sick Children. Pp. 417; 67 illustrations. London: University of London Press.

THIS volume on the medical diseases of children appears as one of a series of medical publications under the caption of London Medical Publications.

The purpose is apparently to place in the hands of students and young medical practitioners a manual of ready reference. For such a purpose, the methodical arrangement of chapters and their subdivisions is admirably adapted. There is a simplicity and avoidance of detail or discussion which is characteristic of the didactic lecture for young students and customary in many text-books of this type.

J. F. S.

DES HAARSCHWUNDS URSACHEN UND BEHANDLUNG. Sanitätsrat DR. S. JESSNER. Seventh revised edition. Pp. 50; Würzburg: Von Curt Kabitzsch, 1914.

THE writer treats his subject in five divisions: alopecia adnata, subdivided into alopecia senilis and alopecia prematura; alopecia

seborrhoica: alopecia areata; alopecia mycetica (trichophytica, favosa); and alopecia symptomatica. Two divisions are made of the symptomatic alopecias; those resulting from changes in the contiguous skin, as from trauma, syphilitic ulceration, erythematous lupus vulgaris, etc.; and those resulting from constitutional diseases, infectious disorders, myxedema, etc.

A favorable prognosis is emphasized in alopecia seborrhoica if the treatment is started sufficiently early. The routine use of soap and water, in addition to salves and lotions, is indicated, according to the writer, in the condition cited in his small volume. The mercury light and the uviole and quartz lamps are mentioned as having therapeutic value in alopecia areata. A considerable number of local applications are given in the text. F. C. K.

SURGICAL DIAGNOSIS IN ILLUSTRATION FORM. By DR. MED. J. CEMACH. 100 tabulations; 10 pages of continuous text; 440 black and colored illustrations. Munich: J. F. Lehman, 1914.

THE patient comes to the surgeon for treatment, but the surgeon's first and chief duty is to determine the cause of the trouble. The solution of this problem usually decides the method of treatment. Special books on differential diagnosis are coming into favor, but frequently fail to emphasize the essential facts. This compendium, in the German language, by Cemach is one of the best that it has been the reviewer's privilege to see. There are only 10 pages of continuous text, but numerous diagnostic tables, every one of which is accompanied by a series of illustrations of the condition under discussion. The purpose is to teach the differential diagnosis, as far as possible, by illustrations which are, in the main, good. Exceptions might be taken to some. For instance, the subacromial and subdeltoid are not two separate bursæ but two names for the same bursa. Such errors are usually minor and do not seriously impair the value of this good book on surgical diagnosis.

T. T. T.

MENDEL'S PRINCIPLES OF HEREDITY. W. BATESON; Honorary Fellow of St. John's College, Director of the John Innes Horticultural Institution. Pp. 413; 48 illustrations. New York: G. P. Putnam's Sons.

ELEVEN years ago Bateson published a little book under the above title but with the subtitle: *A Defence*. In this were included a biographical notice of the then little known Mendel translations

of two of his equally unfamiliar papers and a stirring defence of the principles therein set forth. In 1909 Bateson considered that enough work had been done to make unnecessary a *defensive* presentation of the subject and his fuller and more detailed studies were embodied in a book with the present title. This now appears in its third reprint with but few alterations in the text but with a number of appendices in which some of the more important additions or changes in the subject are briefly presented, pending a contemplated rewriting of the entire book. The additional matter concerns principally the questions of coupling and repulsion, and of the heredity of sex, and is presented in the author's usual graphic and suggestive manner. Bateson's book is the most comprehensive and authoritative presentation of Mendelism in English and is so well known that an extended review is not called for.

C. E. M.

THE ROAD TO A HEALTHY OLD AGE. ESSAYS, LAY AND MEDICAL.
By THOMAS BODLEY SCOTT, M.D. Pp. 104. New York:
Paul B. Hoeber, 1914.

THESE essays have a literary charm which is in keeping with the author's former friendship with Robert Louis Stevenson who affectionately refers to him in the dedication of "Underwoods." Although the book has been written chiefly for the profession the facts are presented in such a simple manner as to be readily comprehended by the laity. In the first chapter he sets up an ideal of "becoming old wisely, honorably, and usefully," and drops a few hints, dietetic and hygienic, for the attainment of such an ideal. In the second he deals with certain pathological conditions of the circulatory system frequently occurring in old age and discusses in considerable detail their prevention and treatment. The third chapter is devoted to the vaccine treatment of the chronic non-tubercular diseases of the respiratory organs that so often cripple old people and shorten their lives. A final brief chapter by his son, Surgeon Gilbert Bodley Scott, R. N., gives an outline of the preparation of vaccines.

T. G. M.

DIE CHRONISCHEN ERKRANKUNGEN DER HINTEREN HARNROHRE
(CHRONIC DISEASES OF POSTERIOR URETHRÆ). By DR. ERICH
F. WOSSIDLE, Berlin. Pp. 155; 82 mostly colored illustrations.
Leipzig: Dr. Werner Klinkhardt.

THIS monograph is in general the most comprehensive and complete treatise on the subject of chronic diseases of the posterior

urethra and its associated organic structures that has appeared. The various phases of the subject are well classified and thoroughly discussed. Although stress has been laid throughout upon the importance and necessity of urethroscopy for the proper diagnosis and treatment of many cases, a just consideration of other clinical diagnostic procedures and methods of treatment has not been neglected. It may be rightly objected that the author should at least allude to the value of the high frequency electrical current (Oudin or d'Arsonval) in comparison with electrolytic and other electrotherapeutic methods for the destruction of polypi, papillomata, etc. Again it may be inquired as to the propriety of devoting so much attention to impotency and prostatic disease to the exclusion of the seminal vesicles. The illustrations, many colored urethroscopic views, are exceptionally meritorious and numerous and deserving of attention by all those interested in this subject.

B. A. T.

DEFENSIVE FERMENTS OF THE ANIMAL ORGANISM. By EMIL ABDERHALDEN, Director of the Physiological Institute of the University at Halle, a/s; English translation by J. O. GAVRONSKY and W. F. LANCHESTER of third German edition. Pp. 242; 11 text figures and 1 plate. New York: William Wood & Co., 1914.

THE great interest which has been aroused by Abderhalden's theory of protective (defensive) enzymes, its practical use in the diagnosis of pregnancy, and the many attempts to apply the theory as a means of diagnosis in diseases of various organs, makes especially welcome an English translation of this noted investigator's account of his labors in this particular field. That interest in the subject discussed is indeed great is shown by the fact that between the appearance of the first German and this translation of the third German edition a period of less than two years has elapsed.

Abderhalden's theory, briefly stated, is, that upon the introduction into the body of substances out of harmony with (foreign to) the blood-plasma, new ferments appear which are capable of transforming these substances into simpler compounds and thus of depriving them of their specific character. The experiments of Abderhalden and his associates support this theory not only in regard to proteins, but in regard also to carbohydrates and fats. Moreover, in pregnancy, Abderhalden has established a definite diagnostic procedure based on the fact that placental products, normally foreign to the blood, enter the blood-stream during the pregnant state and cause the formation of a specific ferment. Other investigators have attempted to apply the same principle to cancer, dementia precox and a large number of other diseases.

In the book before us Abderhalden sketches the development of his theory in its relation to the general principles of metabolism and gives examples of the experimental production of ferments for proteins, fats and carbohydrates. This is followed by a discussion of his biological test for pregnancy and of the possible application to various infectious and organic diseases. Much space is given to the description of the two methods—the dialysis and the optical—of demonstrating the presence of ferments and in connection therewith the author presents in detail the many possibilities of error, which are responsible, he believes, for the contradictory results frequently obtained by those who have used his methods in the study of various practical problems.

In an appendix is presented a complete list (up to November, 1913) of papers on this or related problems. R. M. P.

NUCLEIC ACIDS. THEIR CHEMICAL PROPERTIES AND PHYSIOLOGICAL CONDUCT. By WALTER JONES, PH.D., Professor of Physiological Chemistry, Johns Hopkins Medical School. Pp. 118. London, New York, Bombay, and Calcutta: Longmans, Green & Co., 1914.

HITHERTO no comprehensive treatise has presented systematically our present knowledge concerning the nature and properties of the nucleic acids and this in spite of the fact that they now constitute one of the most satisfactorily elucidated problems of physiological chemistry. This monograph sketches the historical development of the subject and then proceeds to give the present conception of the chemical structure of nucleic acids and of the course of their metabolism in the animal body. The author takes the stand that all the nucleic acids that have been studied are identical either with thymus nucleic acid or with yeast nucleic acid. He considers allantoin as probably the only physiological destruction product of uric acid and considers that human beings have no power to destroy uric acid, in which respect they differ from all the lower animals studied. The views of those who disagree with the author on these and on other points are outlined, and the experimental evidence pro and con briefly described. An excellent bibliography with about 450 references is appended and the work is carefully indexed. J. H. A.

PROGRESS OF MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Observations on the Malarial Parasite.—MARY ROLLEY LAWSON (*Jour. Exper. Med.*, 1914, xix, 451). Previous observations have led Lawson to believe that the malarial parasite is extracellular throughout its entire existence; that it attaches itself to the red-blood cells by means of delicate pseudopodia which encircle and squeeze up into a mound part of the hemoglobin, and finally, that the anemia observed in malarial patients is only to be explained on the assumption that the parasites migrate from cell to cell, destroying one after another. The evidence for this assumption consists in (1) the finding of pigmented parasites free in the blood-serum in various stages of their development; (2) the occurrence of pigmented parasites of the various ages attached to unaltered red-blood cells; (3) the similar occurrence of pigmented parasites attached to decolorized corpuscles called by her "corpuscular skeletons;" (4) the observance of pigmented parasites caught apparently in the act of abandoning degenerated red cells; (5) the finding of corpuscular skeletons alone, which are the expanded decolorized remains of the red cells usually more or less semilunar in shape, granular and staining pink. In the study of a recent case Lawson found over 100 thirty-hour (?) parasites partly on and partly off of the expanded red-blood cells, which showed granular degeneration and in the same smears parasites of the same ages were observed free. Considerable space is devoted to a discussion of why such a picture could not be the result of the technique used in making the smear. Lawson does not believe that in smearing the blood it would ever be possible to reach the parasite if it were submerged beneath the surface of the red cells in order to pull or squeeze it out, at least without damaging that corpuscle itself beyond repair. Arguing

by analogy Lawson concludes that adult forms attach themselves to corpuscular mounds in exactly the same way that younger forms do; in other words, the adult parasite assumes its more or less characteristic ring form solely for the purpose of securing attachment to the surface of the red corpuscles.

On the Effects of Long-continued Overfeeding with Carbohydrates without Protein.—E. GRÄFE (*Deutsch. Archiv f. klin. Med.*, 1914, cxiii, 1) reports carefully conducted experiments on man, the dog, and the swine on the effect of overfeeding with carbohydrates while withholding protein. The results of the experiments are fully discussed and are set forth in tables. The findings were rather unexpected. Gräfe discovered in his numerous experiments on man and animals that in spite of long-continued overnourishment with carbohydrates without protein, there was often not only no gain in weight but even an actual loss. To determine the explanation of this fact, Gräfe made prolonged observations on the effect of the overnourishment not only on the weight, but also on the N-metabolism, water balance, and heat production. It was found that the loss in weight was due primarily to marked loss of water from the body. Coincidentally, there was in all cases a rather considerable increase in oxidation, which was less pronounced in the first few days of overfeeding but became more marked in the second and third weeks. The increase in oxidation amounted to a maximum of 60 per cent. in the swine, corresponding to about one-half of the excess of calories; in the dog it amounted to only 33 per cent., while in man the figures were lowest, though the duration of the experiment was also shorter. It was found that the addition of protein to the excessive quantities of carbohydrates converted the negative water balance at once to a positive. The intensity of the oxidation remained practically unaffected, but in one experiment on a dog there was probably an increased formation of fat from sugar.

Changes in Spinal Fluid in Tuberculous Meningitis.—MANDELBAUM (*Deutsch. Archiv f. klin. Med.*, 1914, cxiii, 92) has continued his work on the spinal fluid of patients succumbing to tuberculous meningitis, and has studied fifteen cases. He finds that the fluid which is clear antemortem becomes cloudy a few hours after death. This turbidity is due to the appearance in the fluid of a large number of endothelial cells which are actively phagocytic macrophages. The cells begin to appear a few hours before death. Tubercle bacilli are found in the cells constantly postmortem, and red cells and leukocytes may also be observed. Recently, Lenk and Pollack have observed that the spinal fluid in tuberculous meningitis is rich in peptolytic ferments, which are active in a dilution as high as 1 to 200. Examination of the peptolytic power of the fluids by means of glycyltryptophan showed that there was a marked increase after death. By using washed cells, Mandelbaum has shown that the endothelial cells contain such an enzyme. Furthermore, he showed that the dura, gray matter, and white matter possess only feeble peptolytic power as compared with the meninges (pia and arachnoid).

Hexamethylenamine as a Source of Error in the Esbach Test.—E. SCHMIZ (*Deutsch. med. Woch.*, 1914, xl, 128) has found that hexamethylentetramine (urotropin) excreted in the urine gives a precipitate with picric acid. When Esbach's solution is employed to determine albumin quantitatively it is evident, therefore, that the reading may be disturbed, if the patient is taking this drug. The precipitate formed is yellow and crystalline. The presence of urotropin in the urine may be determined as follows: 2 c.c. of Esbach's solution are mixed with an equal amount of 15 per cent. KOH, and then warmed until the precipitated potassium picrate is dissolved. Now add 0.5 c.c. of the suspected urine. If urotropin is present there is a change of color from light orange to deep red. If the test is positive, then another method of estimation should be employed. (The inaccuracy of the Esbach solution has been repeatedly demonstrated; Tsuchiya's reagent, which may be substituted for the Esbach reagent, is preferable in every way. Schmiz' findings with regard to hexamethylenamine furnish an additional reason for discarding Esbach's solution.—R. S. M.)

The Relationship of the Function of the Hypophysis Cerebri to Diabetes Insipidus.—C. ROEMER (*Deutsch. med. Woch.*, 1914, xl, 108) reports experiments and clinical observations which tend to support the recent studies of von den Velden and of Farni on the pituitary gland. The latter authors have reported that in at least a part of the cases of diabetes insipidus there is hypofunction rather than hyperfunction of the hypophysis. In fact, they observed a diminished secretion of urine following administration of the posterior part of the pituitary gland. Römer confirmed these observations in experiments on rabbits. The most striking results were obtained with Aubing's colloid extract of the pituitary gland of the ox, though definite decrease of urinary output also followed the intravenous administration of pituitrin (Parke, Davis & Co.) and pituglandol (Hoffmann-La Roche). Recently a case of idiopathic diabetes insipidus came under observation. The patient was a child, aged nine years, who was passing 10 to 11 liters of urine of 1.001 to 1.003 sp. gr. a day. Administration of the colloid extract intravenously was followed for a few hours by a diminished urinary secretion and marked lessening of the somnolence, which had been a prominent feature of the case. Autopsy revealed a tumor pressing on the posterior lobe and on the infundibulum. These observations, with those cited above, show that diabetes insipidus is due to a lack of the secretion of the pars intermedia in some cases at least, and not to a hyperfunction.

The Distribution in and Elimination of Urea from the Body.—MARSHALL and DAVIS (*Jour. Bio. Chem.*, 1914, xviii, 53) point out by a review of the work done up to the present time that estimations of the urea content of organs and the conclusions drawn from them are conflicting and unsatisfactory. Moreover, they call attention to the fact that the retention of urea is a regular occurrence in certain cases of severe nephritis and that there is evidence of an increase also in the urea content of the tissues in cases where the blood urea is abnormally high. Inasmuch as the extent to which urea may be stored in the tissues has never been accurately determined, Marshall and Davis have under-

taken experimentally to determine this, and other points of interest. On the basis of the experimental work reported Marshall and Davis conclude that the modified method of Marshall for the determination of the urea content of tissues gives results quite as accurate as when this method is applied to the study of blood, urine, or spinal fluid. Urea is present in all the organs and tissues of normal animals and its distribution in them is approximately uniform and equal to that of the blood, even when there is an abnormally large amount of urea present. The chief exceptions to this are fats which have a uniformly low urea content and tissues from the urinary tract, which have a high content. The injection of urea solutions intravenously is followed by rapid diffusion into all parts of the body, which is complete within a few moments. It is apparent that the kidneys are capable of eliminating urea with great rapidity, and this rate of excretion in normal animals is directly proportional to its concentration in the blood. The excretion of the urea is retarded by dehydration of the organism. When for any reason the excretion of urea is prevented it would appear that the entire amount formed is stored in the body and there is no evidence of the conversion of urea into other substances under these conditions.

The Effect of Altitude on Blood-pressure.—There is a widespread belief among physicians of the lowlands, says P. SCHRUMPF (*Deutsch. Arch. f. klin. Med.*, 1914, cxiii, 466), that patients with circulatory disturbances should not be permitted to go to the mountains. Though Schrumpf formerly shared this belief, his experience has convinced him that it is fallacious and that many patients with circulatory troubles are actually benefited by a stay at an elevation of two thousand meters or less. The usual reason against altitude is the entirely mistaken belief that the blood pressure will be raised as the atmospheric pressure becomes less. Normal pressure is unaffected by an ascent to two thousand meters. In a group of thirteen patients with slight arteriosclerosis and hypertension, but without serious renal disease, Schrumpf has always found fall in pressure, the decrease amounting to 25 to 55 cm. water. Similar results were obtained in patients with marked arteriosclerosis. In the hypertension associated with chronic nephritis there was a slight fall, less marked than in the non-nephritics. In the arteriosclerotics there was marked subjective improvement with the fall in tension. In "pseudohypertonie" of psychogenic origin, the drop in pressure was even more marked, namely, 45 to 85 cm. water. A group of eight cases of hypotension was studied. In these patients, two to three weeks at an elevation of 1800 meters sufficed to raise the systolic pressure to normal. There was also a rise in the diastolic pressure and in the pulse pressure. In cases of coronary sclerosis altitude is contra-indicated, as is well known. Likewise, patients with decompensation should not be sent to the mountains. Patients with well compensated valvular lesions stand moderate elevations as well as those with normal hearts. Thus, it is evident that altitude has a beneficial effect on blood-pressure, decreasing high systolic and diastolic pressures and elevating those which are below normal, with subjective and objective improvement in the patient's condition. It is advisable in all patients with circulatory disturbances to insist on complete rest the first two or three days after going to higher altitudes.

SURGERY

UNDER THE CHARGE OF

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Free Transplantation.—LEXER (*Annals of Surgery*, 1914, lx, 166) discusses the free transplantation of the various tissues of the body. He emphasizes, particularly, the knowledge and practical use of skin transplantation and, more particularly, of bone. The technique of skin and epidermis transplantation is well known, and various methods are employed. Granulation tissue is better razed with a knife than with a spoon. He always freshens the base. To secure hemostasis, he ligates all visible bleeding vessels and then allows the surface to remain uncovered until there is a visible fibrin formation. He then exerts pressure over the surface with a gauze sponge moistened with warm saline solution. This stops all bleeding. Substitution of epidermis for mucous membrane is not practicable, since infection and secretion interfere with the healing process. Where epidermis is contra-indicated on account of previous cicatrization with shrinkage of the skin, transplantation of skin finds its usefulness. According to Hirschfeld, healing takes place as well with as without the subcutaneous adipose flap. For successful healing to take place, the primary adhesion of the flap is essential. Should this intimate contact and gluing be disturbed within the first twenty-four hours, on account of bleeding on inflammatory transudate, death of the flap usually occurs followed by marble-like areas and cicatrization as a final result. Transplanted hair sheds, regenerate only rarely. Like the hair, finger nails with the contiguous skin do not lend themselves to successful transplantation. Even with favorable nutrition of the nail bed, the shape and growth of the nail are abnormal. The advantage in the use of long strips of epidermis over skin flaps lies in the certainty and rapidity with which repair takes place. The advantage of skin flaps over epidermis strips, rests in the greater persistence of the former, since it contracts less and affords a better cosmetic effect. For this reason Lexer prefers to use skin flaps on the face and fingers. The function of the bone graft and its covering lies in the fact that it replaces the missing tissue and enables the body to build up new bone. For this purpose the transplant is endowed with long life and vigorous powers of regeneration, and the implanted graft retains its shape until the edges of the recipient's defective bone regenerate, in spite of the fact that the implanted bone tissue disintegrates and becomes necrotic. A further advantage in

including the periosteum is that it aids in the cementing of the graft to the wound edges and stimulates invasion by bloodvessels, thus establishing early nourishment. Clinical success in the repair of large denuded bony cavities, can be achieved only by the use of living bone covered by periosteum.

A Contribution to the Operative Treatment of Acute Gastric Hemorrhages.—ALBERT (*Deut. Zschr. f. Chir.*, 1914, cxxx, 398) says that 5 per cent. of gastric ulcer patients die of hemorrhage. Gastro-enterostomy or jejunostomy alone, is easily performed but does not positively provide hemostasis. Excision will stop the hemorrhage, but is too severe an operation. Albert recommends gastro-enterostomy for the less severe cases, as those with chronic recurring hemorrhages, but jejunostomy together with ligation of the arteries at the greater and lesser curvatures supplying the ulcerated areas. When the ulcer is in the neighborhood of the pylorus, the arteries can be ligated in their subserous positions along the greater and lesser curvatures and even those to the duodenum to an extent of about two fingerbreadths. If the ulcer is at the greater or lesser curvature, some distance from the pylorus, the ligation is to be done on both sides of the ulcer. The ligation is especially easy at the two curvatures but is seldom possible on the posterior wall because the vessels are very large and the ulcer has almost always encroached upon the pancreas. The investigations of Kirschner and Mangold showed that complete division of the nerves to the pylorus had no troublesome influence on the normal function of the pylorus. There is little need to fear necrosis of the stomach supplied by the arteries ligated. W. Braun excluded four-fifths of the stomach in dogs without damage. In one patient with cancer of the stomach, Braun ligated the vessels in the greater and lesser curvatures from about a hand's breadth from the cardia to the pylorus preparatory to a resection and then found that the resection could not be done. A gastro-enterostomy was substituted and three weeks after operation there were no symptoms of stomach disturbance and the digestion was better than before the operation.

Chronic Ulcers of the Stomach and Duodenum.—MAYO (*Annals of Surgery*, 1914, lx, 220) divides his experience into three periods. The first period between 1893 and 1900, relates to cases in which operation was done only for marked pyloric obstruction. He refers to the second period, between 1900 and 1906, as that of the growth of knowledge the result of surgical observation; and to the third period, between 1906 and 1914, as that of the development and improvement in diagnosis. The great value of the history and physical findings in diagnosis was emphasized. The relation of the clinical symptoms to the lesion was shown in the light of operative experience, and the value of the purely laboratory examinations of gastric contents were found to have been overestimated. The Röntgen ray gradually won first place in the diagnosis of these lesions and the necessity for the excision of gastric ulcers, because of the menace of cancer, was recognized. 1841 cases of acute and chronic ulcers of the stomach and duodenum have been operated on. The percentage in the last 1000 cases acutely observed showed 73.8 per cent. duodenal and 25.2 per cent. gastric ulcers. The

terminal three-quarters inch of the pyloric end of the stomach is not often involved in ulcer. The more common seat of gastric ulcer is along the lesser curvature, often saddle-shaped. It is more often on the posterior than anterior wall. But whether situated anteriorly or posteriorly, a superficial ulcer at the point of contact often appears on the opposite wall, the "contact" ulcer. The situation of the ulcer, however, may be at any point in the wall of the stomach. Multiple ulcers of the stomach and duodenum, or separate ulcers of the stomach and duodenum exist in about 5 per cent. of the cases. Permanent healing of chronic ulcers of the stomach and duodenum by non-operative means must be of infrequent occurrence. A large number of acute, subacute, and some chronic ulcers are cured permanently, but if they fail to show permanency after a reasonable attempt at cure under ordinary conditions of life, the patients should be treated surgically. The patient with ulcer treated medically is in far greater danger of death from hemorrhage, perforation, obstruction or cancerous degeneration than he is from operation. Gastrojejunostomy is the most generally useful operation for gastric ulcer, especially those with pyloric obstruction. Because of the menace of cancer, all ulcers of the stomach, without regard to their situation, should be excised if possible. As a rule, gastrojejunostomy should be done in addition to excision. In a small percentage of the cases of both gastric and duodenal ulcers there has been a definite recurrence of symptoms and in them it would appear that an actual recurrence of the original ulcer had taken place. A small number of these cases have been operated on and in each instance the source of the trouble proved to be a gastrojejunal ulcer in the suture line of the original gastrojejunostomy.

Gall-stone Ileus.—WAGNER (*Deut. Ztschr. f. Chir.*, 1914, cxxx, 353) calls attention to the fact that we can usually diagnose the presence of acute intestinal obstruction readily enough, but find much difficulty in determining the particular variety or cause. On the basis of four cases operated on and a study of the literature, he made a study of that variety due to gall-stones. The path by which the stone reaches the intestine was shown clearly in his second case; first the development of an inflammation of the gall-bladder and then a pericholecystitis and adhesions between the gall-bladder and duodenum. This is followed by a distension ulceration until a perforation occurs and the stone passes from the gall-bladder into the intestine. Rarely the perforation occurs into the stomach, colon or small intestine. The stone produces signs of acute obstruction most frequently in the lower ileum, less frequently in the jejunum and only in isolated cases in the duodenum or rectum. Most of the patients die of peritonitis due to the distension ulcer at the site of obstruction, often from necrosis of the intestine oralward from the stone. In spontaneously cured cases the stone is required to pass from the anus, in from thirty hours to eleven weeks. The history of gall-stone symptoms may be completely absent or may have occurred so long before as to have been forgotten. An acute onset of the ileus is characteristic, usually, with severe colicky pains, nausea, eructations and vomiting, at first biliary but later fecal. The condition develops most frequently in old women. The stone is usually large. An exact diagnosis is rarely made because the history is frequently

defective. A tumor rarely can be felt and one thinks more easily of the more common causes of strangulation. Early operation is the best treatment. The median incision below the umbilicus is preferable. If the stone is faceted other stones should be looked for in the gall-bladder and intestine.

Special Forms of Extension.—KLAPP (*Zentralbl. f. Chir.*, 1914, xli, 1209) describes methods of extension in cases in which the usual forms, as by adhesive plaster and nail extension, could not be used. A six-year-old boy with a supracondyloid fracture of the humerus, had had applied a circular plaster dressing around the elbow which caused severe pain and swelling of the hand. On admission to the clinic there was a marked hematoma at the site of fracture. There were blebs in the skin filled with bloody serum. The arm to the fracture was swollen, the hand cold, cyanotic, and fingers completely immovable and contracted. The radial pulse could not be felt. A silk suture was passed through the end of each of the four fingers and the ends of the four sutures tied together some distance from the fingers. By means of these without further dressing a five-pound extension was applied to the arm. After three days the radial pulse could be felt and the swelling and cyanosis had subsided. After fourteen days the extension was removed, and the movements of the fingers were considerably improved. After four weeks there is still some induration and brownish discoloration of the finger ends due to the extension. The elbow, hand, and finger movements are free. Klapp therefore recommends this extension treatment in recent cases of ischemic muscle contractures. There is no fear of the sutures tearing through the skin and the finger ends become normal soon after the extension is removed. In a three-months-old child with a congenital defect of the fibula and marked angulation of the tibia, after a tenotomy of the Achilles tendon and osteotomy of the tibia, he was able to apply a plaster bandage in the correct position by means of a similar skin extension to the heel.

Restoration of the Bladder by Means of the Heitz-Boyer-Hovel-Acque Operation.—GREGOIRE (*Journ. d'Urolog.*, 1914, vi, 45) says that the great difficulty in overcoming the disturbances and danger of exstrophy of the bladder comes from the absence of a cavity and of a sphincter. The greater number of operations seek a sphincter in the anal sphincter but without making a vesical cavity. The intestine becomes a cloaca in which the feces and urine mix together. Other operations make a bladder without a sphincter. The detached rectum has been used as a bladder, the sphincter being provided by the anal sphincter. Gregoire did the following operation on a feeble-minded woman, fifty years of age, with destruction of the wall between the rectum and bladder and greater part of the urethra. The abdomen was opened, two ovarian cysts found and a subtotal hysterectomy performed. The rectum was drawn forward and crushed by an angiotribe, at the level of the second sacral vertebra. A double ligature was applied here and the crushed portion of the intestine divided by a thermocautery. The stump of the lower segment was immediately inverted by a seroserosal suture. The superior stump was covered by a gauze compress and laid aside. The two ureters were then transplanted

into the anterior wall of the inferior segment. The rectum was detached from the sacrum and the superior intestinal segment, enveloped in the compress, was insinuated posterior to the rectum to the perineal floor, the abdomen being closed with a drain. The patient was then placed in the lithotomy position, the posterior circumference of the anus incised, the mucosa separated and sphincter isolated posteriorly. The skin and deeper tissues were then incised along the right border of the coccyx to a centimeter from the anus. After going through the levator ani muscle, the upper segment of the rectum was recovered. It had ascended and was found and brought down with difficulty. The rectal musculature was incised longitudinally in the region where the mucosa was separated posteriorly. The upper stump covered by its compress was now pulled through the button hole, the compress removed and the inferior margin of the stump sutured closely to the skin of the posterior wall of the anus and to the mucosa. A drain was placed in the anococcygeal wound. On the fourth or fifth day a blackish discharge escaped from the perineal drain and this soon became frankly fecal. A part of the wall of the stump drawn down, sloughed from excessive traction. This discharge ceased in three weeks and the wound soon healed. From the beginning there was continence of feces and even of gas. The same was not true of the urine. The new bladder seemed to be incontinent, but the mental condition of the patient prevented learning if this was strictly true. The urine did not escape continually but was forced out by the patient with grimaces. There seemed to be an acute cystitis of the rectum. The patient was discharged nearly three months after operation. The mental condition did not permit an endoscopy. There was complete recovery from the operation but the loss of urine continued.

THERAPEUTICS

UNDER THE CHARGE OF

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Intravenous Injections of Sodium Salicylate in the Treatment of Rheumatic Affections.—CONNER (*Med. Record*, 1914, lxxxv, 323) says that with the proper technique and with a chemically pure preparation of the drug the administration of sodium salicylate by intravenous injections is safe, painless, and easily performed. When administered intravenously the drug seems to have a much more pronounced analgesic effect than when given by mouth. The solution for injection is made by dissolving 10 grams of chemically pure crystalline sodium salicylate in 50 c.c. of distilled water which has been freshly sterilized by boiling. The size of the individual dose and the frequency of the injections will vary with the requirements of the individual case. In most cases the dose has been either 15 or 20 grains, and the injections

have been given at twelve- or eight-hour intervals over a period of from three to six days. Occasionally, in robust men, as much as 30 grains have been given at a time, and as much as 120 grains given in the first twenty-four hours without any unpleasant effects whatever. No shock, prostration, or other objectionable constitutional effects have followed this plan of treatment. Conner does not believe that the intravenous method will replace the usual one in the routine treatment of rheumatic fever, but thinks it has a distinct field of usefulness, the limits of which cannot yet be determined. At present this field seems to include cases in which the drug is not well borne by the stomach; those which show little or no improvement under the usual method of administration, and, possibly cases of severe rheumatic inflammation of the eye.

Indication for and Results of Splenectomy for Internal Disease.—KLEMPERER (*Therapied. Gegenwart*, 1914, lv, 1), reports 10 cases of pernicious anemia in which splenectomy was performed as a therapeutic measure. Two of the patients did not survive the operation, but one of these had advanced heart disease and the other had pneumonia before the operation. The remaining 8 cases were in advanced stages of pernicious anemia, but all showed marked improvement in the blood picture and general condition following the operation. In 1 case the improvement was so marked that the result amounts to a clinical cure, while in the others the blood picture, although vastly improved, still shows the characteristics of pernicious anemia. In addition to the benefits that may be obtained in pernicious anemia by the removal of the spleen, Klemperer says that experience has shown that marked anemia of the secondary type, accompanied by enlargement of the spleen (such as occurs in Banti's disease, splenic anemia, and hemolytic jaundice), are often much benefited by removal of the spleen. On the other hand, splenectomy does harm rather than good in leukemia, lymphosarcoma, malaria, syphilis, amyloid and congested spleen.

The Origin and Present Status of the Emetin Treatment of Amebic Dysentery.—VEDDER (*Jour. Amer. Med. Assoc.*, 1914, lxii, 501) discusses the origin of the emetin treatment of amebic dysentery, and gives briefly the experimental evidence that has proved emetin to have true amebicidal action. He says that the emetin treatment is the most effective method we have of treating amebic dysentery at the present time. Of 110 cases treated by this method by twenty-two different observers, 99 were clinically cured, while 11 died. Analyzing the fatal cases, Vedder believes that all were beyond hope of a cure, and says that any amebic dysentery patient who is not moribund can be cured by emetin. The rapidity of the improvement in the cured cases is noteworthy. In many of these reported cases the patients have obtained complete relief from their dysenteric symptoms within a week after the use of very small amounts (from 2 to 3 grains) of emetin. Of 16 cases of hepatitis treated by nine different observers, 16 were cured. These cases have as yet shown no tendency to recurrence, which is so frequent after surgical treatment and evacuation. Several of these cases were treated before suppuration occurred, several after the

formation of pus and without evacuation, and several after evacuation of pus by rupture into the lung or the intestine. Several of these cases had also been treated surgically and by the use of other drugs, such as quinine irrigations, without effect, and were considered practically hopeless before emetin was tried. Vedder says that the final proof as to whether amebic dysentery is permanently cured by emetin can be determined only by observing these cases for a number of years. A large percentage of the cases treated with emetin continue to harbor the ameba (often in the encysted and most dangerous form) in the feces for some time after the clinical cure. In view of this fact it is impossible to state at present that patients treated by emetin will remain permanently cured, yet the prospects of obtaining permanent cures by this method are encouraging. Emetin hydrochloride and the hydrobromide have both been used, but the hydrochloride is preferable, being much more soluble. Vedder prefers a hypodermic administration because of greater safety. Inasmuch as larger doses are distinctly irritating he prefers to give one-third grain three times a day for a period of ten days. In this manner a large amount of the drug can be administered without untoward symptoms. Vomiting has never been reported from the use of emetin in this dosage and the patients feel no general disturbance. After such a course if the patient is clinically cured treatment should be suspended. Any recurrence of dysenteric symptoms indicates a second course. It is undoubted that a great number of amebic dysentery patients become chronic carriers of encysted amebas. These encysted amebæ are not affected by emetin, and Vedder suggests that the amebæ in this stage may be removed by a course of irrigations of quinine or silver nitrate. The results of emetin in amebic disease have been so promising that there has been a tendency to extend this treatment to other diseases. However, experiments have failed to show that emetin possesses any marked therapeutic virtue in bacillary dysentery, syphilis, rabies, or trypanosomiasis.

The Treatment of Cancer with Autolysates.—TUNCKENBEIN (*Müch. med. Woch.*, 1914, lxi, 18) reports remarkable improvement in 15 cases of inoperable cancer following intravenous injection of an autolysate derived from the patient's own tumor. One marked advantage of the treatment is that it acts on both the primary and the metastatic tumors. The most marked benefit was a prompt and marked relief from pain; this relief was very marked in one case, the pains subsiding in a few hours after intravenous injection of the autolysate, although the pain had previously resisted the action of morphine. The author reports the cases in detail, and it is noticeable that the cases influenced by the treatment were benefited in one or two weeks.

The Treatment of Syphilitic Diseases of the Central Nervous System by Intravenous Injections of Salvarsan.—SPOONER (*Boston Med. and Surg. Jour.*, 1914, clxx, 441) believes that it is possible to treat in a satisfactory manner syphilitic diseases of the central nervous system by intravenous injections of salvarsan in an ambulatory clinic. Small doses of the drug are necessary for this purpose, but such dosage yields results. With the exception of six cases placed subsequently on serum treatment, symptomatic improvement has resulted from

thorough treatment in a high percentage of cases of tabes and in all cases of syphilis of the central nervous system. No distinct improvement has resulted from treatment of the few cases of general paresis under observation. Improvement in strength and gain in weight is the rule in those who receive benefit. The relief of lancinating pains in tabes and headache in cerebral syphilis is most striking. Biological and cytological changes (in blood and spinal fluid) indicate that there is an organic basis to this symptomatic improvement. Improvement has been maintained over a long period of time—in many instances for from one to two years. The results of laboratory investigation when obtainable and the amelioration of symptoms correspond. Whereas the failures have been in old-standing cases, it is impossible to show any constant relationship between the degree of improvement and the duration of the nervous lesion. It is noteworthy that the most striking improvement follows the first or second injection. Treatment however, must be persistent and prolonged and should be continued even if all symptoms and laboratory findings have long disappeared. Reactions are infrequent with small doses of the drug. Local accentuations of symptoms which may be explained on the theory of a Herxheimer reaction are disagreeable but usually of short duration. These exacerbations are often followed by distinct improvement in the symptoms. Accidents are rare as a result of the treatment. The most pronounced successes are in those who show evidence in blood or spinal fluid of intense syphilitic infection. The failures have occurred in those showing feeble reactions. Spooner advises this treatment in all cases of syphilitic disease of the central nervous system and it should be abandoned for the serum treatment only when conscientious effort in this simple and safe procedure has failed.

The Comparative Value of Cardiac Remedies.—JANEWAY (*Arch. Inter. Med.*, 1914, xiii, 361) says that in cases of well-compensated mitral disease, in which auricular fibrillation with great tachycardia sets in acutely, the tachycardia can be controlled by digitalis within forty-eight hours with complete relief of the symptoms. Such patients may maintain a very fair working ability for several years under long-continued digitalis medication. It is important that treatment be instituted before marked dilatation of the right heart and general venous stasis have ensued. The three elements contributing to the result in these cases are: (1) The existence of a disorder of the rhythm, against which digitalis is absolutely effective; (2) the existence of a valve lesion, the detrimental mechanical effect of which on the circulation are peculiarly heightened by auricular fibrillation; (3) the acute character of the onset of fibrillation in a heart which would have remained well compensated for years, had not the disturbance of rhythm occurred, and which, therefore, must be considered as having had a good right ventricular myocardium. Next to these acute cases of fibrillation in response to digitalis comes the type picture of gradual cardiac insufficiency with general venous stases and edema. The more these cases conform to the acute type, the more promptly does the control of the tachycardia by digitalis effect a restitution of function. On the other hand, even in rheumatic mitral disease with fibrillation, if the rate be normal or slow, the effect of digitalis treatment

may not be evident until it has been administered for a week or more. In some cases, especially with marked tricuspid regurgitation and liver stasis, it may fail entirely. In other cases the drug acts only after the institution of such accessory measures as the extreme fluid and salt restriction of the Karell diet, which Janeway has found of the utmost value. The choice of a preparation of digitalis is, to Janeway's mind, largely a matter of taste, provided the one used is known to be effective. As to dosage he prefers a moderate dose, equivalent to not over 0.1 gm. of the leaves every four hours, which will give definite slowing of the pulse and diuresis in forty-eight hours in rapid fibrillating cases. This dose he continues until the pulse falls to near 60 or becomes bigeminal; failing this, until absorption of edema is complete, or nausea, vomiting, headache or other toxic symptoms ensue. When any of these evidences of fine therapeutic action is obtained, the drug is stopped and not resumed until increasing rate or pulse deficit, or disappearance of coupled beats, show the heart to be escaping from its influence. Then one-half or three-quarters of the daily amount given before will control all symptoms. In all fibrillating cases with a tendency to rapid rate, after the original digitalis course, Janeway believes the indications for continued so-called chronic digitalis treatment are absolute. He believes that failure to obtain satisfactory results from digitalis therapy in the class of cases just discussed is evidence of an ineffectual preparation, insufficient dosage, or an improper mode of administration. Whenever digitalis fails, a second and then a third trial should be made with a drug obtained from another source. In hypertensive cases of cardiac insufficiency with normal rhythm when the patient develops the picture of chronic passive congestion of the viscera with edema, digitalis is as clearly indicated as it is in fibrillating mitral hearts. Janeway insists that dangerous increase in blood-pressure from digitalis, as used in human beings, is a superstition without any basis of clinical fact. When digitalis alone does not effect prompt improvement in such patients, the caffein diuretics come in as valuable aids. They should be given intermittently in comparatively small doses, 2 gms. of caffein, 10 gms. of diuretin, or 3 gms. theocin, for three doses, and should not be repeated until one or two days have elapsed. In a number of instances Janeway has seen marked and lasting benefit from digitalis in aortic insufficiency where the clinical picture was that of chronic passive congestion and edema.

Antityphoid Vaccination in the Army During 1913.—RUSSELL (*Jour. Amer. Med. Assoc.*, 1914, lxii, 1371) gives charts and tables that show the incidence of and the death rate from typhoid fever in the army from 1907 to 1913, inclusive. These show the steady fall in the number of cases of typhoid fever since the introduction of antityphoid vaccination into the army and especially since compulsory vaccination. Thus, in the entire army of over 90,000 men, only three cases of typhoid fever, with no fatalities, have occurred during the year 1913. It has been claimed that antityphoid inoculation renders the recipient more susceptible to tuberculosis or tends to activate latent tuberculous foci. Russell says that tuberculosis in the army not only has not increased since the introduction of vaccination, but that it has actually

decreased. He says that the conclusion is inevitable that the prophylactic vaccine as used in the army has given almost absolute protection against typhoid fever without producing untoward effects of any character.

Subcutaneous Injections of Emetin in Pulmonary Tuberculosis.—RAEBURN (*British Med. Jour.*, 1914, 2778, 703) was led to try the effect of subcutaneous injections of emetin hydrochlorid upon hemorrhages in pulmonary tuberculosis by the favorable results reported by Flindin and Joltrain. Raeburn used this method of treatment in over forty cases with excellent results. In addition to the effect of emetin in controlling hemorrhage, he noted a very beneficial effect upon the cough and especially a marked diminution in the amount of sputum. He does not consider that emetin has any effect on the tubercle bacillus but believes that it is a valuable remedy for reducing congestive conditions in the lungs and therefore it is both a preventive and curative agent in pulmonary tuberculosis.

Splenectomy in Blood Diseases.—MÜHSAM (*Deutsch. med. Woch.*, 1914, xl, 377) says that the consensus of opinion is that splenectomy if done early enough is curative in Banti's disease. The results of splenectomy in 14 cases of hemolytic jaundice have been exceptionally good. He relates his personal experience with this operation in 11 cases of pernicious anemia. Five of these patients died, 3 soon after the operation and 2 sometime after the removal of the spleen. The blood-picture has improved in all of the remaining cases, but still retains the characteristics of pernicious anemia. These patients are apparently well and have gained materially in weight and strength.

The Treatment of Insomnia in Cardiac Insufficiency.—FRÄNKEL (*Therapie d. Gegenwart*, 1914, lv, 200) reports eight cases of cardiac insufficiency in which he tried various remedies for sleeplessness. He believes that the intravenous use of strophanthin is the most rational measure to control insomnia when it is a marked feature in cardiac disease. In cases of cardiac asthma where the patients get little or no rest, he has found that strophanthin is very effective and more certain of results than any form of digitalis by mouth. He believes that morphin should be given regularly for insomnia in chronic cardiac decompensation only when digitalis and strophanthin have proven to be ineffectual.

Hexamethylenamin.—McGUIGAN and V. HESS (*Arch. Int. Med.*, 1914, xiii, 853) believe that after the administration of hexamethylenamin, free formaldehyd appears only in the gastric juice and acid urine and not in other secretions or in the blood. The liberation of formaldehyd results from the acid reaction only and not from cell action. Even if it were liberated in other localities it would probably exert no beneficial action because of its reconversion or rapid oxidation into injurious products. Combined formaldehyd as hexamethylenamin does not decompose readily until an acid medium is reached, when the action is that of weak formaldehyd. The only apparent indication for the internal administration of the drug, therefore, is in infection of the urinary tract.

PEDIATRICS

UNDER THE CHARGE OF

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Vaccination Against Diphtheria in Infants.—P. ROHMER (*Berlin klin. Woch.*, 1914, li, 1350) undertook to determine whether it is practical to increase the immunity of infants to diphtheria by vaccinating them with v. Behring's diphtheria antitoxin. He offers the following results of his investigation as a general preliminary indication of the possibilities. The strongest antitoxin of v. Behring was used, TAVI. Injections were made intracutaneously in the forearm near the elbow, the amount injected each time being 0.1 c.c.m. The strength of the solutions were: for the first injection, a dilution of 1 to 20; for the second, 1 to 10 or 1 to 5; and for the third the undiluted antitoxin was used. The reaction thus accomplished was inferred to indicate that the child was "sensitized" and the last dose given was repeated about fourteen days later as an "antitoxin-producing" injection. Cultures were taken from the nose and throat of all cases to determine the presence of the diphtheria bacillus and the antitoxin content (diphtheria) of the blood was estimated before, and from five to eight days after the injection. The tests were made on sixteen infants, differing in age, constitution, and nourishment. The age varied from two and a half months to two and a half years. From the stand-point of antitoxin production the results show the children divided into two groups according to age. Infants under four or five months showed no increase in this antitoxin content whatever, whereas all the children above that age showed an appreciable increase. The former group, however, showed primarily a fairly high antitoxin content. It suffices, however, to say that infants under four or five months may be excluded for the present, at least, from the necessity of this form of vaccination. The intensity of the local reaction was the same in infants of five to eight months as in those of two to four months, but the former group showed increase in the antitoxin content, the latter did not. Infants older than nine months showed a stronger local reaction under similar doses but only a slight general reaction, but showed no higher increase of antitoxin content than the five to eight months' infants. The results apparently show that it is practicable to effect an immunity in infants by vaccination with v. Behring's diphtheria antitoxin.

The Treatment of Infectious Conditions in Childhood.—TOBLER (*Dutsch. med. Woch.*, 1914, xl, 1297) states that while a diagnosis is theoretically the first point in the treatment of a condition, in actual practice, especially among children, it is often impossible to follow this rule. He states the importance of treating primarily the general symptoms caused primarily by an infection with some disease. Chill, fever, anorexia, thirst, mild delirium, stupor, and vomiting are general primary symptoms of infection which must be met with appropriate treatment to preserve general vitality. As to the diet during fever, Tobler believes that systematic under-nourishment is detrimental

and that the physiologically poor value of albuminus as fuel unfits them for an exclusive diet. A diet rich in fats puts too much work on the digestive organs, so that the carbohydrates really come to the front as the best diet to rely on. In older children with fever he suggests the following: zwieback or wheat-bread, flour-soup with egg, cold pudding of maize and fruit juice and apple compote. In addition during prolonged fevers, rice, potatoes, noodles, and macaroni. In infants with fever the diminished tolerance to nourishment and the tendency to diarrhea modify considerably the dietary scheme outlined for older children, and large dilutions of the nourishment, and the intermediate use of sweetened weak tea is indicated. For the treatment of fever in infants the bath in water of medium temperature is best. In high fevers, water should be 35° to 36° C., and by slowly adding cold water, brought to 34° to 32° C. In older children cool packs are preferable at 20° to 30° C. Where general disturbance of the child is undesirable, cool, moist clothes can be laid on hips and limbs and frequently changed, or light sponging attempted. Antipyretic drugs are of decided value at times, especially in headache, delirium, etc., and should be given only during increase, never during decrease of the fever curve. Tobler mentions the salts of potassium and aspirin as suitable antipyretics for infants and children. For circulatory weakness in infections Tobler uses caffeine preparations in mild conditions and injections of camphor oil and preparations of digitalis in the more severe conditions. In "meningismus" a lumbar puncture, by withdrawing 5 to 10 c.c. of fluid, usually gives sufficient relief.

Intramuscular Injections of Antitoxin in Diphtheria.—J. D. ROLLESTON and C. MACLEOD (*British Jour. Diseases of Children*, 1914, xi, 289) review the work done by various investigators on the various methods of administering antitoxin. It was shown that more rapid absorption occurred by the intramuscular method than by the subcutaneous. Morgenroth and Levy showed also that after eight hours in intramuscular injections the antitoxin content of the blood came very close to that after intravenous injection. Since 1909 intramuscular injections have largely superseded subcutaneous in German hospitals. The practice has apparently been confined to the German speaking countries. The gluteal region and the outside of the thigh are the usual points selected. The authors report their experience in using this method on 339 patients at the Grove Hospital. There were 261 completed cases of diphtheria to whom 324 injections were given. Injections were given in the vastus externus muscle. The largest dose given at one time was 20,000 units or 50 c.c. The following advantages of this method are as follows: A uniform and high concentration of antitoxin in the blood is effected. It is less painful during the injection and subsequently no abscesses occurred in any of the cases. Rashes and serum phenomena occur as in the subcutaneous method. There were 15 deaths, 11 of which were due to toxemia. There was a comparatively low rate of paralysis, especially of the severe kind. For these reasons intramuscular injection of antitoxin in diphtheria deserves to supersede all other methods of administration. The average dose used in this series was 12,459 units, the dosage by this method has been decidedly smaller, especially in severe cases than it had been for the subcutaneous methods.

OBSTETRICS

UNDER THE CHARGE OF

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Placental Ferments in the Blood of Pregnant Women.—ECALE (*Archiv. Mensuelles d'Obs.*, March, 1914) has made extensive study to determine the action of ferments in the blood of the pregnant woman. Like others, he finds that this reaction is present from the first month of gestation, and usually ceases about three weeks after the birth of the child. Its intensity is not influenced by the period of gestation, nor by the nature of the placenta, when that comes from the normal patient. The action of blood-serum taken from the cord upon the placenta is often lacking, and when it is present it is often much more feeble than the action of the blood-serum of the mother upon the placenta. In the case of a dead fetus or retention of the placenta the reaction may be negative. In ectopic pregnancy a positive reaction is always obtained when the ovum is living, but negative if the ovum has died. In the presence of albuminuria or eclampsia the method does not give positive results. In pernicious nausea the reaction is diminished or disappears. As regards patients when not pregnant, in 70 out of 100 there is no reaction; in the remaining 30 a reaction to some extent was obtained. These positive results were chiefly obtained in women who had had free hemorrhage, or absorption from a collection of blood or pus, or who were victims of malignant disease. In many cases an abnormal reaction was caused by some fault in technique, or the use of serum containing traces of hemoglobin. In certain conditions of disease this reaction may be vitiated by the presence of albuminoid bodies other than those obtained from the placenta.

Pregnancy in Uterus Bicornis.—MARSHALL (*Jour. Obst. and Gyn. British Empire*, April, 1914) reports an interesting case where pregnancy was present in the right half of a bicornate uterus. This had reached six months in development. From the left side came a purulent discharge, and the condition at first was thought to be a suppurating dermoid. Under rest in bed and antiseptic douches the discharge almost disappeared and abortion occurred. This completely destroyed the septum, and when the patient was discharged there were two openings in the cervix and one central body of the uterus without partition.

Extra-uterine Pregnancy with Tuberculous Peritonitis.—CROOM (*Jour. of Obs. and Gyn. British Empire*, April, 1914) reports the case of a patient admitted to hospital with a large abdominal tumor containing fluid. The patient was weak and emaciated, with high pulse and moderate fever. No evidence of pregnancy could be found by abdominal examination. By internal examination the condition of the cervix

was such as to lead to the suspicion of pregnancy with tuberculous peritonitis. The patient's condition was so bad that operation was declined, and death soon followed. At autopsy, extensive tuberculous disease was present, with extra-uterine pregnancy at the position of the left tube. The pregnancy had gone nearly to term and the placenta was attached inferiorly and posteriorly along the rectum. The original implantation of the ovum had been on the lower and posterior aspect of the left tube. The tube had ruptured, but evidently without occasioning disturbance.

The Prophylactic Use of Vaccines in Puerperal Sepsis.—In the *British Med. Jour.*, June 6, 1914, CHAMTALOUPE describes his researches and experience in the prevention of puerperal sepsis by vaccines. As regards the pregnant woman, he, with others, has found that various sorts of pathogenic bacteria are present in the vagi during pregnancy. In sepsis the streptococci and staphylococci with allied bacteria are most frequently present. In collecting material from the interior of the uterus for diagnosis, the writer has found the following method useful: He sends to the physician in charge a glass tube, containing a wire swab. A mark is made on the wire handle, when the swab end is just within the uterine end of the glass tube, another mark 2 inches further away, so that the practitioner knows just how much of the swab end is projecting beyond the glass tube when in the uterus. The uterine end of the glass tube is lightly plugged with cotton, to which a string is attached. The whole swab is placed in a good-sized test-tube, plugged with cotton, sterilized in the autoclave to avoid the charring of the cotton or the string. After sterilization the glass tube is removed from the test tube, and its uterine end dipped in sterile molten paraffin, which cools and forms an impervious cap. Instructions are issued with the swab outfit, stating that the uterus should be drawn down with forceps and the os exposed to view. After cleaning the os with sterile gauze the swab is passed until the end reaches the fundus. It is then withdrawn an inch and traction applied to the string, which pulls away the paraffined cotton cap. The swab is carefully pushed out of the glass tube by means of its projecting outer end and the interior of the uterus well swabbed. Finally the swab is drawn into the glass tube and that replaced in the sterile test-tube, in which it was sent out. If in town, the swab is carried in a vertical position to the laboratory, and if in the country it is carefully packed in that position and sent by the quickest means available. This method has proven successful and is sufficiently simple to be used in the average case. In some cases blood cultures can be taken and are of great value. In one, the streptococcus and bacillus coli were found in intra-uterine cultures and present in the blood. The writer distrusts all commercial imported sera, and he has not seen good results from antistreptococcus serum, although freshly prepared. He further believes that the indiscriminate use of vaccines in all sorts of cases is exceedingly injurious. He employs vaccines sensitized to the individual patient, with good results. While some investigators use living sensitized vaccines, he has not risked that, but kills bacteria employed in making these vaccines. He urges the prophylactic use of these vaccines and illustrates it by the report of an epidemic of five cases of puerperal sepsis in a

maternity hospital. The first arose in a multipara, and the method of infection could not be ascertained. The intra-uterine use of the swab showed streptococci and staphylococci. The patient did well with the use of streptococci vaccine. Four other cases in the same institution contracted the infection, but all recovered. Two remaining cases developed fever soon after confinement and were immediately treated with vaccines. The temperature promptly fell. The patients then remaining in the institution, but not yet confined, were given vaccines, and passed through labor and the puerperal period without complications. Chamtaloup believes that Health Departments, which now give antityphoid vaccines and diphtheria antitoxin for general use, should add to this sensitized streptococci vaccines for prophylactic use in obstetrics. His experience indicates that doses of 100, 250, and 500 million of this vaccine, may be given at 48-hour intervals, ten to fourteen days before the expected date of confinement.

The Treatment of a Uterine Abscess by Sensitized Bacilli.—BROUGHTON-ALCOCK reports in the *British Med. Jour.*, June 6, 1914, a case recently treated at the St. Louis Hospital of Paris, as follows: The patient was a married woman, aged fifty-five years, who complained a long-continued vaginal discharge of pus. On examination a probe could be passed through the cervix into an abscess cavity, which had developed following a hysterectomy. The pus from this cavity contained pure cultures of *Bacillus proteus*. The patient's treatment was limited to daily vaginal douches for cleanliness, and seven injections at intervals of three or four days of a culture of the bacilli made from the pus. The first dose being equal to 100,000,000, the last to 2,000,000,000. The bacilli were heated to 60° C. for an hour before administration. Slight reaction followed the injections on the eighth day after the last injection, and sensitized vaccine was prepared from the patient's blood. At this time a vaginal examination was again made, and the *Bacillus proteus* found in lessened quantity, but pure culture. On the tenth day after the last injection of dead bacilli the sensitized vaccine was given, one injection weekly for four weeks, the dose from 400,000,000 to 1,000,000,000. Very slight reaction followed and the abscess cavity was washed out with dilute antiseptic solution. After the fourth vaccine injection the discharge of pus entirely ceased, but for security four other injections were given. At the date of writing, six months had elapsed, the patient remaining in excellent conditions.

The Treatment of Hemorrhagic Disease of the Newborn by Direct Transfusion of Blood.—LESPINASSE (*Jour. Amer. Med. Assoc.*, June, 13, 1914) reports fourteen cases of hemorrhage in the newborn treated by direct transfusion of blood. The arm of the donor is placed beneath the left thigh of the infant, the palmar aspect of the hand uppermost, so that the radial artery of the donor and the femoral vein of the baby may be joined. During transfusion the child's color greatly improves, it becomes vigorous, gains from eight to fourteen ounces in weight and is usually strong enough to nurse. By weighing the baby before and after transfusion, the amount of blood received must vary from eight to fifteen ounces. These patients are not hemophiliacs and they usually recover rapidly after transfusion, and do well. The smallest

baby treated weighed four pounds. The period of transfusion varies from five to fifteen minutes. The vessels used were the radial artery in 7 cases, and the forearm vein in 7 cases on the donor; on the baby, the femoral vein was used in 4 cases, and the jugular in 10 cases. The father was the donor in 10 cases, the mother's half sister in one, and a non-relative in 3. There were no deaths from bleeding, but two died from syphilis.

Twin Pregnancy Intra-uterine and Extra-uterine, with Living Fetus.—BOGDANOVICS (*Zentralbl. f. Gyn.*, 1914, No. 22). The patient was in her third pregnancy, her first having been twins with dead children of the same sex. The second pregnancy terminated in normal labor. During the second month of the third pregnancy she had violent pain in the lower abdomen with shock. Pregnancy continued, however, until near term, when she gave birth in spontaneous labor to a male fetus 45 cm. long. An hour later she complained of severe pain in the lower abdomen, which gradually ceased and returned the following day. She was admitted to hospital with a diagnosis of ectopic pregnancy. On examination a fetus could be palpated in the abdomen, and heart sounds could be heard. This was confirmed by operation, a living fetus being found in a sac without amniotic liquid, with pulsating cord and placenta partly adherent to the omentum. The child was rapidly delivered and the placenta was removed with unusual facility. The child was weak and ill developed, although equal in length to the twin born spontaneously, but lived but a few moments. The tubes and ovaries were apparently normal; a corpus luteum was found in the left ovary. The ova had evidently come from the left ovary and between the birth of the twins twenty-two days had elapsed. While simultaneous intrauterine and extra-uterine pregnancy are not infrequent, at the same time this case is unusual because both children went to viability, and the fetus delivered from the abdomen survived the spontaneous birth of its fellow for a short time.

The Treatment of Eclampsia by Abdominal Cesarean Section.—PETERSON (*Amer. Jour. Obst.*, June, 1914) publishes a review of 500 cases of abdominal Cesarean section for eclampsia. The statistics show an improvement of nearly 50 per cent. accompanying the general improvement in obstetric surgery. The lowest mortality given by abdominal Cesarean section for eclampsia is 13.15 per cent. The article contains many interesting statistics, but practically it is of value to know that these cases were not under the care of skilled obstetricians in most instances in which eclampsia had developed, and many of them had had several convulsions. It is impossible to judge how thorough and accurate had been the treatment of toxemia among these cases. It has long been known that toxemia and not eclamptic convulsions form the important element in the morbidity and mortality of this condition. When the statistics are compared with the results of the treatment of toxemia culminating in eclampsia, by bleeding, lavage of the stomach and bowel and the administration of calomel and salines, followed by delivery by forceps or version, where labor begins, and by section, if labor does not begin, it is seen that the mortality reported where eclampsia is treated by section, is twice that where the toxemia

is treated, and delivery by section is employed only when labor does not develop, and the treatment of toxemia fails to control it. In hospital the prompt treatment of toxemia with aid to labor as required, gives a maternal mortality of between 6 and 7 per cent.

Central Placenta Previa Treated by Hysterotomy.—FEKETE (*Zentralb. f. Gyn.*, 1914, No. 22) describes a case of central placenta previa, having severe bleeding before the pains began, treated by delivery by abdominal section, followed with the removal of the uterus. The patient was a multipara with a normal pelvis. The child in vertex presentation. Hemorrhage had been severe, the patient was exsanguinated, the hemorrhage temporarily ceased, but pains did not develop, and tampons had been applied to control the bleeding. Fearing a return of the hemorrhage the uterus was emptied by abdominal incision, its vessels immediately ligated, and the uterus removed. The patient made a good recovery. Barsony describes the case of a patient, eight months pregnant, having had hemorrhage at intervals for a week and treated by the use of the tampon, successfully delivered by abdominal Cesarean section. The patient was a primipara with an undilated and long cervix.

GYNECOLOGY

UNDER THE CHARGE OF

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Radium Treatment of Uterine Hemorrhage.—Some remarkable results in the treatment of uterine hemorrhage, due in some instances to fibroid tumors, in others to various conditions, by means of radium have recently been reported by KELLY of John Hopkins (*Jour. Amer. Med. Assoc.*, 1914, lxiii, 622). Although the series is rather small, comprising in all but 39 cases, the results as recorded equal or excel those obtained in the German and French clinics, which for some years have been expending so much energy on this line of work. The cases are divided into four groups, as follows: (1) Adult women with marked menorrhagia or metrorrhagia, but with no disease of the pelvic organs, except perhaps a slight enlargement of the body of the uterus, the endometrium being microscopically normal. Of these, there were 8 patients; amounts of radium varying from 60 to 268 mg. were applied for periods of from two to twenty-four hours. In only one case was more than one application necessary; in 2, there was no recurrence of bleeding whatever after the first treatment; in the remaining 5, one normal period occurred after treatment, to be followed by complete amenorrhea. (2) Young girls suffering from hemorrhages, presenting the same anatomical findings as Group 1 or 3. Of these there were 5 cases, ranging in age from thirteen to twenty-three years. In all there was severe anemia, with a bad cardiac lesion in one. The dosage

used here was much smaller, varying from 12 to 60 mg., applied for five to twenty-four hours. In three instances the treatment was followed by the reestablishment of normal menstruation; in one case the periods became irregular, but never excessive, and in the fifth (the heart case) complete amenorrhea was produced. (3) Elderly women having the polypoid condition of the endometrium commonly termed "polypoid endometritis," associated with bleeding. In this group there were likewise 5 cases; 4 were relieved at once by a single application, the fifth case was not relieved, and hysterectomy was performed five days after treatment owing to severe hemorrhage. (4) This is the most important group, comprising 21 patients with good-sized fibroid tumors. The ages varied from thirty-two to fifty-nine years; excessive bleeding was present in all but two, one of whom was several years past the menopause. In 16 of these patients complete amenorrhea was produced within one to two months, in some instances immediately after the treatment. In 2 others the remarkable result of the persistence of normal menstrual periods with complete disappearance of the tumors is claimed, and in almost all cases a marked reduction in the size of the tumor was seen. Only one case was a complete failure, and required surgical intervention. *Technique:* Kelly lays stress on the fact that the radium must be applied directly into the interior of the uterus, and not in the cervix or vagina. His procedure is to give the patient gas, make a thorough examination under the anesthetic, and then curette the uterus. The radium is introduced into the uterine cavity in a glass tube, which is encased in 0.5 mm. of platinum, 0.5 mm. of zinc foil, and 0.3 mm. of rubber. The amounts used varied in different cases from 12 to 560 mg. and the exposures from one and one-half to forty-eight hours. (In expressing the amount, this is always given in terms of radium element, no matter what the salt actually employed.) Kelly says that his general tendency has been to increase the amount of material and reduce the time, finding that he gets better results in this way. He is extremely enthusiastic, and believes that this type of treatment has a great future in store for it.

Treatment of Uterine Prolapse by Vesico-uterine Transposition.—In a paper presented at the last meeting of the American Gynecological Society, WATKINS, (*Surg., Gyn., and Obst.*, 1914, xix, 392) says that since introducing this type of operation in 1898, he had performed it about 275 times, but has only been able to trace 104 of the patients. There was no recurrence of the cystocele in any case, but in 13 some recurrence of the uterine prolapse had taken place; this consisted in protrusion of the fundus uteri or of the cervix. Watkins believes that these recurrences were due to faulty judgement, the operation not being modified to meet the requirements of the individual case. Such partial failures, however, can easily be remedied by a second operation, the main difficulty, the cystocele, having been permanently relieved. He emphasizes the fact that in performing this type of operation it is important to individualize; for instance, if the uterus is very large, a portion of the body should be excised, chiefly the anterior wall, enough of the posterior wall being left to close the hernial opening through which the bladder protrudes. The cervix should not be amputated

routinely, but this should be done when it is much hypertrophied, and especially when it is very long, and protrudes through the vaginal orifice. A report on a much smaller series of cases of the same operation has also been recently presented by NOVAK (*Surg., Gyn., and Obst.*, 1914, xix, 412). During the past five years he has done the transposition operation on 26 patients, of whom he has been able to keep track of 16. All of these women were suffering from complete prolapse, and with one exception the results have been highly satisfactory. Of the 26 patients, 9 were still within the child-bearing age; in all of these, sterilization was performed by excising about an inch of each tube near the uterus and burying the stumps in the broad ligament. Novak takes the ground that while ordinarily this operation is not indicated in the woman not yet past the menopause, in certain cases it is justified; if a woman has had a number of children, is suffering with extensive prolapse, and desires above all else to be restored to health and strength, regardless of the possibilities of future pregnancies, he thinks it is not only justifiable but clearly indicated, since in his opinion no other procedure assures the result as does the "Watkins-Schauta" operation. The one case in which Novak did not attain success was in a woman who had had a complete prolapse for fifteen years; on attempting to repair the perineum, a most important adjunct to the interposition operation proper, it was found that all trace of muscle tissue had disappeared, and there was nothing to be brought together but fascia. The prolapse eventually returned, but in a somewhat different form from that which had occurred previously; the uterus now came down bodily as it were, with its long axis at right angles to that of the vagina, but still maintaining its position beneath the bladder. There was no prolapse of the latter ahead of the uterus, and the patient was permanently relieved of much of her urinary disturbance.

Amenorrhea and Tuberculosis.—It is well known that a condition of amenorrhea is often found in tuberculous women, and also that the genital organs of such subjects often present an infantile condition, but whether the tuberculosis actually causes any specific changes in the generative organs themselves, which in turn are the direct cause of the amenorrhea, is not so clear. This is a rather difficult problem to solve, as the organs in these cases are not often available for histologic examination, without which a definite determination of the condition is impossible. SCHIFFMAN (*Arch. f. Gyn.*, 1914, ciii, 1) has had the opportunity of carefully studying the organs from two patients of this class. The first was a woman, thirty-five years of age, who died following a panhysterectomy performed on account of osteomalacia. At autopsy a few scattered tubercles were found on the peritoneum and in some of the abdominal lymph nodes; examination of the uterus showed extensive evidence of old, healed ulcerations with calcification, a partial atresia of the uterine canal, and a few typical tubercles. The author thinks that the healed areas of ulceration undoubtedly represent old tuberculous foci. The second patient was thirty-nine years of age, and like the first, had never menstruated. At operation for a cystic ovary, a diffuse peritoneal tuberculosis was found, with tubercles also on the genital organs. The latter were extirpated *in toto*, and on sectioning the uterus this was found to be practically

a solid structure, with complete atresia of the cavity. No definite tuberculous foci were found in the uterus, but such were present in the tubes and ovaries. The author considers the first case an example of *healing*, the second of *healed* uterine tuberculosis, which in both instances would have entirely escaped detection had not the histologic examination of the extirpated organ been made. He was not able to determine, however, whether the failure of menstruation to appear at any time in these women was actually due to the tuberculous process in the uterus itself, or to a primary hypoplasia of that organ, which made it a *locus minoris resistentiæ* for the development of tuberculosis. In Case I, which appears to be a fairly recent process, he thinks the latter explanation the more probable, whereas in Case II the process may well have existed even before puberty, and hence have been the direct cause of the amenorrhea.

Dangers of Radium in Uterine Cancer.—In view of the great enthusiasm which has of late been manifested in many quarters over the results obtained with radium in the treatment of uterine cancer, particularly of the cervix, it is well that occasionally attention should be drawn to the untoward results that are sometimes seen, and not merely to the brilliant successes. Two cases recently reported by MEYER (*Zentralbl. f. Gyn.*, 1914, xxxviii, 1092) are of interest in this connection, as they illustrate the danger of serious infection following the intracervical application of radium. The patients were thirty and sixty-eight years of age respectively; the former was suffering with a beginning, the latter with an advanced and inoperable carcinoma of the cervix. Following the application of a radium container in the cervical canal for a number of hours in each case, a severe para-uterine inflammation, involving the entire pelvic connective tissue on the left side, developed in the younger woman, with eventual resolution; in the older woman, however, a fulminant sepsis occurred, which soon resulted fatally. At autopsy, the entire uterus was found transformed into a pus sac, with necrotic wall and completely disintegrated cervix. The author believes that in each instance the infection arose from the pathogenic organisms practically always present in these cases, and liberated by the irritating action of the radium, as by any other form of intra-uterine manipulation.

Syphilis of the Bladder.—Since the first case of vesical syphilis to be definitely diagnosed by means of the cystoscope was reported in 1900 by Matzenauer, about 20 cases of tertiary, and several of secondary syphilitic lesions in the bladder have been recorded in the literature. To these, GAYET and FAYRE (*Jour. d'Urol.*, 1914, vi, 35) now add three more, and discuss our present knowledge of the subject. The chief symptoms of vesical syphilis are pain in the bladder region, frequent and painful micturition, and *hematuria*. The last named is the most important, and is practically always present, sometimes appearing merely at the end of each act of micturition, sometimes being profuse and constant, at others irregular and fitful in appearance. Cystoscopic examination shows in some instances a pedunculated or sessile mass closely resembling a polyp, in others multiple papillomata of varying sizes, in others, again, numerous areas of ulceration, all

these lesions being located chiefly in the region of the trigone. Their gummatous nature is shown by the rapidity with which they disappear under antisyphilitic treatment, after resisting all forms of local therapy. The first of the authors' personally observed cases occurred in a man, sixty-six years of age, a tabetic with chronic retention and a slight cystitis. He was suddenly seized with severe hematuria, which persisted until treatment with mercury, iodides, and neosalvarsan was instituted, when it rapidly disappeared. Cystoscopic examination showed the presence of multiple ulcerations, which finally became completely cicatrized under the treatment. The second case was in a woman, fifty years of age, with a distinctly syphilitic history and a positive Wassermann. She was seized rather abruptly with frequent and painful micturition, and hematuria. Cystoscopic examination showed a perfectly healthy bladder above the trigone; in that region, however, was a large, rounded protuberance, resembling greatly an enlarged median prostatic lobe. The mucosa covering this was red, congested, and showed numerous small ulcerations and pittings; at one point there were a number of small papillomata. Three injections of neosalvarsan, given at weekly intervals, caused immediate cessation of the hematuria and other symptoms, with a gradual and progressive disappearance of the vesical lesions, as was demonstrated by successive cystoscopic examinations. Case III was also in a woman, thirty-five years of age, who some years previously had had a definite chancre with secondaries, and also gonorrhea. She likewise was suddenly seized with hematuria and dysuria. Cystoscopic examination showed a congested trigone, with a median projection resembling a prostatic lobe, but without ulcerations. No local treatment of any sort was given, but under mercurial inunctions and the administration of iodine internally, there was a rapid disappearance of symptoms, with amelioration of the objective vesical lesions. The patient was lost track of before these had entirely healed, however, as it was impossible to convince her of the necessity for further treatment after the symptoms were relieved. The author considers that these three cases illustrate well three different stages of the disease, Case III being the least, Case I the farthest advanced. He emphasizes the importance of bearing in mind the possibility of a syphilitic etiology of cases of this sort, for if the diagnosis is missed, local therapy, which is useless, will be persisted in, instead of the specific treatment, which is absolutely curative.

OTOLOGY

UNDER THE CHARGE OF

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Anomalies of Ossification in the Human Petreous Bone and their Relation to the So-called Otosclerosis.—In eleven of a series of two hundred temporal bones subjected by MANASSE (*Archiv. f. Ohren-*

heilkunde, 1914, vol. xcv.) to a searching examination for the detection of pathological evidences there were found peculiar and uniformly characterized islands of cartilage in the labyrinth capsule; they were visible to the naked eye, of a rounded or irregular contour, and were situated, with a fair degree of symmetry, between the oval window and the middle whorl of the cochlea, and consisted of hyaline multi-cellular cartilage with occasional fine traversant fibres. The main body of the cartilaginous structure containing fine cretaceous dust and occasionally cretaceous masses. In juxtaposition to these islands, but without genetic relationship, were small areas of new bone with medullary cavities, in the neighborhood of these areas there was, as a rule, atrophy of the membranous labyrinth. As these deviations from the normal were found at all ages, from infancy upward, the author is led to regard the condition as a congenital arrest of development with an interesting analogy to the changes in the cases of otitis chronica metaplastica, namely, origin in the labyrinth capsule, with the same local predilection, the same binaural symmetry, the presence of new bone in the neighborhood of the cartilage islands, and the corresponding localized atrophy of the membranous labyrinth; conditions which would point to a relationship, in causation, of the two forms of labyrinth disorder.

Occupational Impairment of Hearing Artificially Produced.—In a continuation of his experiments, previously reported, HOESSLI (*Zeitschrift f. Ohrenheilkunde*, vol. lxix, p. 3) used his artificial boilermaker's shop, consisting of a suspended section of iron drain pipe, swinging free and struck by a succession of mechanically actuated hammers. The guinea-pigs, as in the previous experiments, were subjected in the iron pipe for a period of eight weeks, twelve hours daily, to the continuous sound of the hammer blows, both ears being open; as a part of the experiment also in some instances, the floor of the pipe, within, was covered by a carpet of felt 2 c.e. in thickness, another series of animals exposed to the noise within the pipe had one ear previously tightly stopped. By comparison of the volume of noise to which the animals were subjected with actual conditions in boiler shops, the author found this experimental noise to be much the weaker which served to explain the slowness of manifestation of the induced labyrinthine changes; the first pathological change in the cochlea was noted at the end of three weeks, but at the end of ten weeks the organ of Corti was virtually destroyed. It was, moreover, evident from these experiments that the sound transmitting apparatus of the middle ear was the medium through which the destructive disturbance found admission to the labyrinth, for the tightly stopped ears remained intact and the thick felting had no protective influence whatever. Protection for the human ear under occupational conditions in continuous loud noises can be effected only by safeguarding of the sound transmitting apparatus by firm closure of the external auditory canal.

On the Reëducation of Hearing.—In the opinion of LAIMÉ (*Ann. des Mal. de l'Oreille*, vol. xl, p. 4), auditory reëducation is one of the otological questions of the day, a question as to the possibility, in default of favorable results of treatment, of ameliorating the condition of

the deaf and of controlling the advance of processes which make for a further limitation of an important special sense. The various attempts toward a favorable solution of the question have had their point of departure from a common ground, the reëducation of the defective organ of hearing by its subjection, in varying degrees, to different classes of sounds. The methods employed for auditory reëducation are divisible into two general groups, the first dealing with the audition of artificial or mechanically-produced sounds, the second availing itself wholly of the sound of the human voice and articulate language. In the first method is included a great variety of sounds of varying timbre and intensity, tuning-forks, sirens, pipes, whistles, and a variety of instruments electrically agitated for the purpose of maintaining a definite and controllable continuity of sound. One of the objections to the employment of sound sources of a mechanical kind is the prevalence of metallic overtones and the injurious effects upon the membranous labyrinth of prolonged exposure of the auditory apparatus to tones of this class as shown by Siebanmann, Hoessli, and others. The second method relies solely upon the instrumentality of the human voice, to the compass of which the human auditory apparatus is especially adjusted, a method which has found its foremost exponents in Austria and North America, some of whom couple the auditory reëducation with the visual study of the component movements of the lips and face. In extreme cases the vocal reëducation should begin with the simple vowel sounds and extend to the introduction of individual consonant checks and later to their combination in spoken words and sentences, while even in cases of a moderate, monaural, impairment of hearing the reëducation is of value as an adjuvant to others, established, forms of local treatment.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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Cellular Constants, Water.—MAYER and SCHAEFFER (*Jour. de Physiol et de Path. gen.*, January 15, 1914) have shown some interesting facts in connection with cellular constants, beginning with water, and its equilibrium in the tissues. The cellular constituents being colloidal complexes, appear in a protoplasm which is a gel: the lipoids are not

confined to cell membranes but are contained in the protoplasm. Protoplasm being a mixture (differing for the type of cell) of albuminoids, lipoids, salts, and water (the cellular constants). Mayer and Schaeffer endeavored to determine upon what the amount of water depends. As far as inhibition of water is concerned, the lipoids act as limiting factors; and cholesterine has a particular power of its own. If fatty acids only or cholesterine alone be present, they prevent the absorption of water; if a mixture of lipoids and cholesterine be present, it renders the lipoids penetrable by water and so lessens this prevention. The more cholesterine and albuminoid gel mixed with lipoids contains, the freer will be its inhibition of water. The water capacity of different tissues varies within narrow limits, and water is a cellular constant; the order of ability to imbibe water is always the same, thus, lung and brain-tissue, kidney, muscle, liver. The water capacity of tissues in general is greater according as the cholesterine is greater in relation to, first the fatty acids, and second, the lipoid phosphorus. Mayer and Schaeffer's observations bear out the statement that the inhibition of tissues increases with lowering of the temperature; also that the red corpuscles of various species are more easily hemolysed the higher is their lipocytic coefficient, that is, the relation of cholesterine to lipoid phosphorus, and tissues swell in water according to the same law.

Labor and Anaphylaxis.—Heide's theory that the onset of labor is the result of an anaphylactic process, while ingenious, is not borne out by the latest work on the subject, that of KOLMER (*Jour. Med. Res.*, January, 1914). Heide considered that the mother was gradually sensitized by fetal toxins, that an antibody is thus gradually produced, and that labor is the result of anaphylotoxin split off by the effect of the toxic substance and the antibody. The administration of serum from pregnant women at term into the veins of those about to fall into labor is negative, but serum separated from the placental blood and injected into patients close to term succeeded in starting the pains, or if not in instituting the pains, at least in increasing pains already present but weak. Kolmer's work with guinea-pigs and serum from pregnant pigs injected subcutaneously into other pregnant pigs at term was without positive result. The same result was obtained when the serum of mother pigs was collected a few minutes after the birth of their young and injected into animals near term. Serum from young pigs immediately after birth, and even from young pigs removed by abdominal section, gave no effects upon pregnant pigs close to term. The extracts of ground placenta was administered without any immediate results. Pregnant pigs were given intravenous injection of serum from human placental blood without result. Finally human placental serum was administered to eight human patients near term with no effect upon the uterus, and with scarcely any effect upon the temperature, pulse, and respiration. In such a case it is difficult to avoid some result, owing to mental impression.

Cytology of the Blood in Passive Immunity.—DOUGLAS reports (*Jour. Path. and Bact.*, 1914, xix, 33) a study upon the cellular content of the blood after the use of various sera. It has been well known that upon the introduction of bacterial antigens into animals a

response may be observed, not only in the development of antibodies, but also in the change in the numerical blood-picture. Most commonly a leukocytosis accompanies the appearance of the antibodies. Metchnikoff attributed considerable importance to this leukocytosis in the belief that some of the antibodies in the serum had their origin in the destroyed leukocytes. Douglas carried out a series of observations upon the actual change in the blood-picture upon the introduction of homologous and heterologous sera. The error in the observations was controlled as nearly as possible in first establishing the mean daily and individual variation of the leukocytes, red cells, and hemoglobin. On inoculating a healthy man with 10 c.c. of normal horse serum a leukocytosis of 13,400 reached its maximum within twenty-six hours, and declined to about normal in four days. The inoculation of the same individual with 2.5 c.c. of diphtheria antitoxin gave rise to a comparable leukocytosis in the same period of time and disappeared with equal rapidity. It would appear, therefore, that the leukocytosis is in response to the foreign serum, and is similar to that produced by other proteins containing antibodies. Upon the introduction of a third quantity of serum (antistreptococci) little or no leukocytosis was obtained. The author suggests that an immune body may have been developed by the repeated use of the serum, which prevents leukocytosis, rather than that the serum itself contains a body-producing leukopenia. The response in the production of leukocytosis is mainly by the polymorphonuclear leukocytes. The change in the number of leukocytes in rabbit blood was not parallel to the results in man. A leukopenia developed upon the injection of normal and immune horse serum. No evidence was found that the antibodies as such have any influence upon the cytology of normal blood of either man or rabbits.

The Excretion of Urinary Solids in Nephritis of Scarlet Fever and Diphtheria.—The types of nephritis which were investigated by KIN-LOCH (*Jour. Path. and Bact.*, 1914, xix, 77) were the acute glomerular and acute interstitial which he found regularly in scarlet fever and diphtheria. In scarlet fever the glomerular disease was often associated with acute interstitial changes. The kidney lesions are to be viewed as the result of the toxic action of the kidney rather than as a disordered metabolism in the body. Thirty-three cases of nephritis were carefully studied chemically during the course of the disease and in them the (1) urinary nitrogen, (2) chlorides, (3) phosphates, and (4) sulphates were determined. *Water:* In glomerular nephritis of scarlet fever and diphtheria there is rapid diminution of the quantity of water secreted which, however, in diphtheria steadily increases after the initial fall, while in scarlet fever the diminished output is long maintained. In true interstitial nephritis of both of these diseases no diminution of urine other than that explained by an extra elimination of water by lungs and skin occurs. *Nitrogen:* Both the percentage and daily output of nitrogen is diminished in the glomerular nephritis of scarlet fever, while no definite change is observed in that of diphtheria. The nitrogen is freely eliminated in the interstitial nephritis of both diseases. *Chlorides:* An immediate and long-continued diminution of chlorine occurs in glomerular nephritis in scarlet fever, while the

output is free and regular in the interstitial nephritis of both diphtheria and scarlet fever. A diminution of the chlorine occurs at the onset of glomerular nephritis and diphtheria, but with the early diuresis it is at once increased. *Phosphates*: The daily output of phosphates is low in both forms of disease. The variation of the output of the other urinary constituents does not materially alter the excretion of phosphates. *Sulphates*: The elimination of the sulphates remains relatively high even when upon the sulphur-rich protein being first broken down.

Myelinosis and Xanthomatosis.—CHALATOW (*Virchow's Archiv.*, 1914, ccxvii, 351) and his school of Russian associates have, from time to time, brought interesting studies upon some phases of the fat problem before us. It was during a series of feeding experiments in which they offered a variety of protein diets to rabbits that they noted the development of curious fatty deposits in the tissues of organs and arteries. It was at first thought that the results were obtained through the agency of the foreign protein offered. Subsequently, it was found that the results were dependent upon the fat, lipoid and cholesterin content of the food. They therefore continued their experiments in feeding pure cholesterin, by which similar fatty changes were produced in many organs. In a closer study of this process Chalатов comes to the conclusion that the cholesterin or cholesterin esters are taken up by different tissues according to definite laws governing the cell functions. By feeding cholesterin in unusual quantities, cholesterin esters are deposited in the liver, adrenal, spleen, bone marrow and intima of aorta, and under unusual conditions in the kidney. On the one hand (bone marrow, spleen and connective tissue), these deposits are the result of active phagocytosis by definite cells of these organs when the cholesterin compounds are freely circulating in the blood. This deposit by phagocytosis he speaks of as xanthomatosis. On the other hand, he points out that an active function on the part of the liver and cells of the cortex of the adrenal is the taking up of neutral fats and lipoids with which cholesterin may enter into combination when free fatty acids are also present. This taking up of cholesterin is thus a passive process and is distinguished under the term myelinosis. To what extent this classification can be applied to the human is not yet clear in that the conditions under which greater or less amounts of cholesterin appear in the blood, is not determined.

ERRATUM.—On page 475, line 5 of the summary, in the article by Joseph L. Miller, M.D., in this JOURNAL for October, 1914, 2 milligrams should be 2 *grams*.

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ORIGINAL ARTICLES

A COMPARISON OF THE RESULTS OF THE PHENOLSUL-
PHONEPHTHALEIN TEST OF RENAL FUNCTION WITH
THE ANATOMICAL CHANGES OBSERVED IN
THE KIDNEYS AT NECROPSY.

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AMONG the most important questions that come before the physician are the ever-recurring inquiries: Are the kidneys the seat of chronic disease, and, if so, how extensive is the process? What is the outlook?

For the past four years we have used the phenolsulphonephthalein test of Rowntree and Geraghty in a considerable variety of conditions in the medical wards of the Johns Hopkins Hospital, and as a result of our observations we have come to regard the procedure as one of considerable value both in the diagnosis and prognosis of renal disease.

Most of the results which have been reported by those who have made use of this method have been based upon clinical observations alone. Occasional necropsies have been described, but nowhere, so far as we are aware, has there appeared any large series of consecutive clinical observations followed by necropsy.

Here and there there are reports, on the one hand, of great variations in the test made from time to time in individual cases, and on the other hand of instances where an approximately normal or even high excretion of 'phthalein has been observed in patients who have died shortly and unexpectedly thereafter with all the signs of an uræmia. In some of these instances, notably the cases reported by Foster, necropsy has revealed what was regarded as extensive chronic renal change.

It seemed to us, therefore, that further light might be thrown upon the situation by a consideration of those fatal cases occurring in the medical service of the Johns Hopkins Hospital in which, after the 'phthalein test had been made during life, a necropsy with careful microscopical study of the kidneys has followed. The fact that many of these cases were presented at the Clinical and Pathological Conference, where a definite opinion was expressed by the clinician as to the nature of the case before he was aware of the results of the necropsy, has added considerably to the interest of the work.

Dr. Winternitz, who has for some years been engaged in the study of the pathological anatomy of nephritis, has been so good as to go over all the specimens and to express his conception of the anatomical nature of the process without previous information concerning the clinical history of the case. An anatomical classification of the material was thus made from a purely objective standpoint. The clinical histories of the patients were then thoroughly analyzed and the results of our functional tests were considered in their relations to the anatomical changes in the kidneys and to the conditions existing at the time when the tests were made.

There were fifty-four cases followed by necropsy in which the 'phthalein test was made during life. The material was classified anatomically as follows:

Advanced chronic nephritis	20 instances
Chronic nephritis of moderate extent	6 instances
Cloudy swelling in association with grave acute infections	6 instances
Severe acute nephritis	1 instance
Amyloid kidney	1 instance
Hypernephroma (unilateral)	1 instance
Chronic passive congestion (cardiac disease)	20 instances

ADVANCED CHRONIC NEPHRITIS. The anatomical changes here observed were those of a progressive chronic inflammatory nephritis with more or less granular atrophy in gross, and microscopically, adhesive glomerulitis, hyaline glomeruli, a greater or less amount of interstitial change—infiltration, œdema, scarring. Acute terminal changes—hemorrhages, exudate, cellular infiltration, epithelial swelling, and degeneration—varied in extent.

In these 20 patients, as may be seen in the accompanying table (Table I), 33 estimates of the 'phthalein output were made, the figures varying from 0 to 38 per cent. in two hours.

TABLE I.—Advanced Chronic Nephritis.

No. of cases.	Period before death.	Percentage of 'phthalein in two hours.
3	10 days	7.0 per cent.
3	9 days	3.1 per cent.
8	12 days	trace
11	5 days	0
18	7 days	18.0 per cent.
21	8 months	24.0 per cent.
21	57 days	35.0 per cent.
21	41 days	36.0 per cent.
21	23 days	34.0 per cent.
21	18 days	16.0 per cent.
23	4 months	10.0 per cent.
23	28 days	trace
24	105 days	20.0 per cent.
24	72 days	trace
24	62 days	trace
27	6 days	37.0 per cent.
29	14 days	7.0 per cent.
31	3 months	18+ per cent.
33	4 days	0
38	3 days	0 (1 hour)
39	3 days	38.0 per cent.
II.	6 days	15.0 per cent.
III.	5 days	0
IV.	3 weeks	6.9 per cent.
IV.	13 days	16.6 per cent.
VI.	23 days	trace
VI.	2 days	13.0 per cent. 1 hour
X.	40 days	26.0 per cent.
X.	31 days	trace
X.	30 days	trace
X.	day of death	trace
XV.	4 days	slight trace
XVI.	43 days	1.5 per cent.

The test was made *within a week before death* in 11 cases, the excretion in two hours varying from 0 to 38 per cent. The percentage of 'phthalein output was as a rule very low—under 18 per cent. The two instances (Cases 27 and 39) with a higher excretion were patients who died respectively of a dissecting aneurysm and a hemiplegia, accidents coming on in the course of a nephritis which had not as yet reached a stage of decompensation.

The test was made *within a month, and over a week before death* in 7 patients. Here the excretion of 'phthalein in two hours varied from a trace to 34 per cent. Patient 21, in whom the excretion was highest, namely, 34 per cent., twenty-three days before death, was an instance of chronic nephritis in a woman of sixty-four with great cardiac insufficiency which unquestionably hastened death. Other functional tests made in this patient showed, also, more favorable results than has been the rule in instances in which the terminal stage of the nephritis has been reached without the intervention of cardiac failure. The test was made at periods from *one to eight months before death* in 5 patients, the excretion varying from 1.5 per cent. to 35 per cent.; it was above 20 per cent. only in Case 21—the patient with cardiac insufficiency above referred to.

Among all these patients records above 36 per cent. were obtained

in but three instances—Cases 21, 27, and 39. Two of these records, each in the thirties, were obtained in the patients dying respectively from a dissecting aneurysm and hemiplegia. The third instance was the case of myocardial insufficiency above referred to where death was associated with hydrothorax and extensive dropsical manifestations. Here also the excretion of 'phthalein fell to 16 per cent. eighteen days before death.

In these patients the renal changes had not presumably reached a stage at which decompensation and uræmia were imminent.

The *manner of death* in these 20 cases was from uræmia in every instance with the exception of Patients 27 and 39—who died suddenly from the rupture of a dissecting aneurysm and hemiplegia respectively. In Case XVI there was a terminal meningitis, but this had been preceded by unquestionable uræmic manifestations.

In almost all patients there was cardiac hypertrophy of greater or less extent, but in only three was death in any direct sense due to cardiac failure (Cases 21, 31, and VI).

The *urine* in all of these instances was of low specific gravity, and toward the end scanty although there was generally a history of preceding polyuria. Albumin was present generally in a moderate quantity. In several cases the albumin was abundant at the end in association with ischuria and acute terminal changes. The sediment was, as a rule, scanty, consisting of hyaline and granular casts and occasional red blood corpuscles. In two instances (Cases 23 and 24) where there was anatomically more epithelial change, epithelial casts were also found in the urine. In but two instances (Case 29, the hemiplegic, and case IV) was the specific gravity at all high. Case IV was an instance with rather rapid clinical course and a good many acute anatomical changes. Here also there were, toward the end, numerous hyaline, epithelial, and blood casts.

The *maximum blood pressure*, as shown by the following table, was elevated in almost every instance.

BLOOD PRESSURES.	
Case 3	95
Case 8	235
Case 11	140 to 175
Case 18	180 to 205
Case 21	240
Case 23	130 to 153
Case 24	216
Case 27	170 to 180
Case 29	130 to 140
Case 31	225
Case 33	167 to 138
Case 38	188
Case 39	200 to 80
Case II.	226 to 236
Case III.	230 to 80
Case IV.	115 to 175
Case VI.	180 to 260
Case X.	180 to 220
Case XV.	170 to 220
Case XVI.	142 to 160

The one instance (Case 3) in which the blood pressure was low is worthy of special note. The patient, a boy of twelve, was admitted to the hospital complaining of polydipsia and polyuria of several years' duration. For two years he had suffered from pains in his legs, rather sharp in character and interfering with his walking; probably from his description, muscular cramps. The physical examination showed a pale boy with rather dry skin and no demonstrable cardiac hypertrophy. The radial arteries were, however, palpable; the maximum blood pressure was 95; the eye-grounds showed no changes. The urine on entry amounted to about 2500 c.c. in twenty-four hours; specific gravity, about 1005; no albumin; no formed elements in the sediment. The 'phthalein test a week after entry, showed a total excretion in two hours of but 7 per cent., and on the following day but 3.1 per cent. Within a day or two the quantity of urine began to diminish, a trace of albumin appeared, and occasional hyaline and granular casts were found in the sediment. The boy became dull and drowsy and, nine days after the last 'phthalein test, died in uræmic coma.

At necropsy the kidneys were found to be exceedingly small and granular, the cortex greatly thinned. On microscopical examination there was little cortical substance left, most of the glomeruli being completely degenerated and represented by small hyaline masses. This is the most striking instance that we have had of the value of the 'phthalein test. Without it we might well have failed to recognize the nature of the case.

FURTHER TESTS OF THE RENAL FUNCTION. In 9 of these instances further tests of renal function were made. The incoagulable N. in the blood was estimated fifteen times in 7 patients.

In six tests made in five patients *within a week before death* the incoagulable N. was:

Case 21	0.5	grammes per litre.
Case 23	1.8	" "
Case X.	1.876	" "
Case 23	2.0	" "
Case 33	2.0	" "
Case 18	2.1	" "

In nine tests made in 5 patients *at longer periods before death* the incoagulable N. was:

Case 21	8 months	0.4	grammes per litre.
Case 21	52 days	0.48	" "
Case 21	40 days	0.43	" "
Case X.	14 months	0.9	" "
Case X.	31 days	0.84	" "
Case X.	30 days	0.864	" "
Case 31	65 days	1.0	" "
Case 23	28 days	0.88	" "
Case VI.	23 days	0.63	" "

The two instances (21 and VI) in which rather low figures were obtained were both cases in which there were grave cardiac compli-

cations and chronic passive congestion, instances in which, although the renal changes were grave, it is yet very possible that they had not reached an extent sufficient of itself to have induced uræmia.

The *lactose* elimination was suppressed or greatly delayed and diminished in all the 9 cases in which it was tested.

The *chlorides* were studied in 6 patients. In three (11, 31, and VI) the elimination was rapid and complete with polyuria (vascular hyposthenuria). The test was made respectively five, sixty-five, and twenty-three days before death.

In 3 cases (18, 27, and XV) one week, seventy-five days, and four days respectively before death the *chlorides* were in part retained. In the first case there was tuberculous pleurisy and peritonitis; in the second, at the time of the test, there was general anasarca and ascites; in the third, an instance of very marked renal change, there was slight œdema.

Iodide of potassium was eliminated in forty-eight hours or less in Cases 18 and VI. It was delayed in Cases 11 (seventy-two hours), 21 (fifty-four hours), 31 (seventy-two hours) and XV (seventy-two hours).

RELATION OF THE PERCENTAGE OF 'PHTHALEIN EXCRETED TO THE LENGTH OF SURVIVAL. The percentage of 'phthalein excreted in two hours was 20 or over in 9 tests (6 cases); longest survival, eight months.

The percentage of 'phthalein was from 10 to 20 in six tests (6 cases); longest survival, four months.

The percentage of 'phthalein excreted in two hours was under 10 in sixteen tests (12 cases); longest survival, seventy-two days.

The percentage of 'phthalein was a trace only in seven tests (4 cases); longest survival, seventy-two days.

The 'phthalein was wholly suppressed in four tests (4 cases); longest survival, five days.

These results are quite in accord with those with which we have met in this clinic in the past four or five years in cases which have not come to necropsy. In no instance of grave chronic nephritis have we failed to find a material diminution in the 'phthalein excretion. In not a single instance in all the studies made at this clinic by Rowntree, Geraghty, Mrs. Winternitz, Fitz, Baetjer, and Snowden have we met with an instance such as those reported by Foster, in which an excretion approaching normal was found in grave chronic nephritis shortly before death. The study of these cases in which we have been able to make the anatomical control, tends to support our previous impression that the test is one of considerable diagnostic value. This study further reveals in rather a striking manner the progressive diminution of the 'phthalein excretion with the advance of the disease. This is so definite as to give the test a considerable prognostic significance.

The anatomical observations suggest that in a good many instances

the terminal event which was almost invariably uræmia, was ushered in by acute renal changes which did not manifest themselves by any striking alterations in the urine. In many of these instances, a few days before death or at the onset of uræmia, the 'phthalein was excreted in but a trace. It is not impossible, however, that a month previously the percentage might have been considerably higher—20 per cent. or even more. Nevertheless, we are considerably impressed with the consistency with which a low 'phthalein output is found in chronic nephritis of any essential degree, and we feel that in the absence of chronic passive congestion the 'phthalein test gives us important diagnostic and prognostic help.

CHRONIC NEPHRITIS OF MODERATE EXTENT. There were 6 cases of chronic nephritis of moderate extent. Of these 5 (Cases 4, 13, 17, 20, and XIV) were associated with a high degree of chronic passive congestion due to cardiac failure. The other (Case 13) was an instance of tuberculous polyserositis with a considerable degree of cardiac insufficiency.

The renal changes in these patients were not extensive, a few glomerulo-capsular adhesions, but little scarring, some exudate with red blood corpuscles in the glomerular spaces. The kidneys showed little gross deformity. In Case XIV, an instance of verrucose endocarditis, the changes were however, more marked and acute than in the others.

The *urine* in all instances was scanty, the specific gravity, however, tended to be rather below normal, excepting in Case XIV, where it ranged from 1020 to 1026. The albumin varied from a trace to a considerable amount. In Case 17, an instance of dilated heart with grave passive congestion and acute endocarditis, the albumin at the end was 0.9 per cent.

The 'phthalein output in two hours, as shown by Table II, varied from 16 to 42 per cent.

TABLE II.—Chronic Nephritis of Moderate Extent.

No of cases.	Period before death.	Percentage of 'phthalein in two hours.
4	9 days	39.5 per cent.
13	7 months	22.0 per cent. (3 hours)
13	5½ months	32.0 per cent.
17	32 days	23.0 per cent.
20	12 days	42.0 per cent. (3 hours)
IX.	18 months	36.0 per cent.
XIV.	1 day	16.0 per cent.

The test was made *within a week of death* in but one instance when, on the day before death, it was 16 per cent.

The test was made *between one and two weeks before death* in 2 instances, when it was respectively 39.5 and 42 per cent. in three hours.

In Case 13, an instance of tuberculous polyserositis with cardiac

failure, the output seven months before death was 22 per cent. in three hours, and 32 per cent. in two hours one month and a half later when the patient was in an improved condition.

The *chlorides* at the time of the first test were well excreted; the lactose was excreted in twelve hours; urea, 0.6 grammes per litre; catalase, from 14.2 to 31.

In Case 20, twelve days before death, the lactose was excreted in eleven hours; K.I. in sixty-two hours, while the incoagulable N. was 0.5 per litre of blood.

In Case IX, eighteen months before death, with a 'phthalein of 36 per cent., the lactose excretion was much delayed and the urea in the blood was 0.8 grammes per litre.

The *blood pressure* in this series, as will be seen by the following table, was not strikingly high, owing possibly to the condition of the heart.

BLOOD PRESSURES.

Case 4	125 to 160
Case 13	140 to 210
Case 17	190
Case 20	90 to 110
Case IX.	110 to 140
Case XIV.	112 to 130

On the whole, this group represents older individuals than those in whom more advanced nephritis was found, individuals whose weakened hearts have been less able to resist the hypertension of a developing nephritis. Death, therefore, has occurred from circulatory failure at an earlier period of the renal disease. The analysis of the ages of these 6 patients shows that with one exception they were all over 40, the average age amounting to 47+, while the average age of the 20 patients with advanced chronic nephritis was but 38.8, despite the fact that one patient aged 71 is included in this list.

CLOUDY SWELLING. There were five instances of cloudy swelling occurring during severe infections. The nature of the infection was:

Pneumonia and gangrene	Case 1
Acute endocarditis	Case 2
Osteo-myelitis and abscess of the knee	Case 6
Syphilis, bed-sore, bronchopneumonia and gangrene	Case 7
Miliary tuberculosis	Case 34

The microscopical changes in the kidneys were not extensive—swelling and granular degeneration of the epithelium, engorgement of the capillaries with the occasional escape of a few red blood corpuscles into glomerular space or tubules.

The percentage of 'phthalein excreted in two hours varied, as may be seen from Table III, from 20 per cent. on the day of death (Case 2) to 50 per cent. forty-five days before death (Case 6).

TABLE III.—Cloudy Swelling.

No. of case.	Period before death.	Percentage of 'phthalein in two hours.
1	9 days	27.0 per cent.
2	day of death	20.0 per cent.
6	6 months	37.8 per cent.
6	10 days later	29.7 per cent.
6	45 days	50.0 per cent.
7	20 days	33.0 per cent. (5 hours)
34	9 days	28.0 per cent.

The test was made *within two weeks before death* in three instances (Cases 1, 2, and 34), the 'phthalein excretion varying from 20 to 29 per cent. In Case 2, in which the output was but 20 per cent. on the day of death, the actual renal changes were not more marked than in the other instances but there was grave chronic passive congestion. In Case 34 the epithelial degeneration was more extensive than in any other case in this group and the 'phthalein output nine days before death was 28 per cent.

The test was made at a period *from twenty days to several months before death* in 2 instances, the 'phthalein excretion varying from 33 per cent. in five hours to 50 per cent. In the former instance, however, the test is of little value, owing to the long period of time over which it was made and to considerable uncertainty which existed as the proper saving of the specimens. The variations in the records of Case 6 are interesting. The patient suffering from abscess of the knee and osteo-myelitis was febrile at the time of the first two tests (37.8 and 29.7 per cent.). At the time of the third test (50 per cent.) he was afebrile and in a much better general condition.

In all of these cases the *urine* was rather scanty, of normal or high specific gravity, the albumin varying from a trace, with a few hyaline and granular casts in the sediment, to a large amount with hyaline, granular, epithelial, and blood casts (Case 2, acute endocarditis). Excepting in Case 2, where there was grave cardiac insufficiency, and in Case 34, acute miliary tuberculosis, anasarca was absent or an unimportant factor.

Our *clinical diagnosis* as to the renal condition was "cloudy swelling" in Cases 1, 6, and 7; in Case 2, "chronic nephritis with an acute exacerbation;" while in Case 34 a diagnosis was not recorded before the result of the necropsy was known.

In one instance not included in this list there was widespread epithelial necrosis (Case 5). This was a case of syphilis of the aorta with valvular insufficiency, extreme cardiac dilatation and chronic passive congestion. There was a terminal peritonitis and colitis. The 'phthalein test, however, was made nearly a month before death and was interesting only for its association with chronic passive congestion, in which group the case is classified.

As we consider these figures then it is clear that a terminal cloudy swelling may be associated with considerable diminution in the 'phthalein output.

SEVERE ACUTE NEPHRITIS. There was one instance (Case 10) of severe acute nephritis, a man of forty-eight, with ulcerative endocarditis and general septicæmia with a pneumo-streptococcus; anæmia; purpura; pulmonary, splenic, and renal infarcts; terminal broncho-pneumonia, pleurisy; and death in coma. The *blood pressure* was 135.

The *kidneys* were large; the cortex swollen; the parenchyma pale. Microscopically there was evidence of a grave acute nephritis with much œdema, catarrhal and exudative glomerulitis, and extensive epithelial degeneration.

The 'phthalein excretion four days before death was but a trace in four hours and the urea in the blood was 1.2 grammes per litre.

AMYLOID KIDNEY. There was one instance of pure amyloidosis, a woman of thirty-three with an old syphilis, complaining of dyspnoea on exertion for five months and swelling of the extremities for a month. She was very anæmic. The *blood pressure* was rather low, ranging from 92 to 124.

The *urine* was very scanty, showing from 0.4 to 1 per cent. of albumin and a specific gravity of from 1012 to 1015, with occasional hyaline casts. Two days before death the patient became stuporous and comatose.

Ten days before death the excretion of 'phthalein in two hours was but 1.2 per cent.; *two days before death* but a trace was observed.

The kidneys at autopsy showed characteristic amyloid disease with extensive glomerular change and slight interstitial fibrosis.

HYPERNEPHROMA. In Case 30 a large irregular tumor was palpable in the right renal region. The ureters were catheterized, and from the right side no 'phthalein was obtained; from the left, 17 per cent. was excreted in fifteen minutes. The left kidney was found to be hypertrophied; the right was almost entirely destroyed, consisting largely of neoplastic tissue.

CHRONIC PASSIVE CONGESTION. There were 20 instances in which the kidneys anatomically showed changes suggesting only chronic passive congestion. Clinically these were all cases of cardiac dilatation and insufficiency.

The main lesion in each of these cases was:

Fibrous myocarditis	8 cases	(Cases 9, 12, 16, 22, 32, 36, V, VIII)
Syphilis of the aorta	7 cases	(Cases 5, 10, 14, 25, 26, 37, VII)
General arterio-sclerosis	2 cases	(Cases 19, 35)
Emphysema and pulmonary induration	2 cases	(Cases XI, XII)
Adherent pericardium	1 case	(Case XIII)

As may be seen by Table IV, the excretion of 'phthalein in two hours varied very greatly according to the degree of cardiac compensation, ranging from a trace to 71 per cent.

TABLE IV.—Chronic Passive Congestion.

No. of case.	Period before death.	Percentage of 'phthalein in two hours.
5	29 days	28.2 per cent.
9	6 months	25.6 per cent.
9	68 days	58.6 per cent.
9	10 days	59.0 per cent.
10	13 days	30.5 per cent.
10	3 days	25.4 per cent.
12 (active diuresis)	4 months	72.0 per cent. (3 hrs. 50 m.)
14	20 weeks	37.0 per cent.
14	12 weeks	22.0 per cent.
16	40 days	48.0 per cent. (3 hours)
19	93 days	50.0 per cent.
22	14 days	31.0 per cent.
25	11 weeks	71.0 per cent.
25	3 days	55.0 per cent.
26	4 months	24.0 per cent.
26	7 days later	63.0 per cent.
32	38 days	48.0 per cent.
35	3 days	28.3 per cent.
36	35 days	trace
36	29 days	38.0 per cent.
36	1 day	trace
37	5 days	69.0 per cent. (2½ hours)
V.	1 day	16.1 per cent.
VII.	6 months	16.0 per cent.
VII.	1 week later	36.0 per cent.
VII.	1 week later	45.0 per cent.
VIII.	1 year	50.0 per cent.
VIII.	8½ months	39.0 per cent.
VIII.	12 days	54.0 per cent.
XI.	3 days	45.0 per cent.
XII.	3 months	49.0 per cent.
XIII.	2 months	61.0 per cent.

In nine cases the percentage of 'phthalein excreted in two hours was under 30 per cent. (Cases 5, 9, 10, 14, 26, 35, 36, V, VII). In all of these instances there was grave cardiac decompensation. The nature of the change was as follows: In 4 cases (5, 10, 14, 26) syphilis of the aorta with aortic insufficiency and its sequels.

In 4 cases (9, 35, 36, VII) fibrous myocarditis with dilatation.

In 1 case (V) a fibrous myocarditis associated with chronic endocarditis and mitral insufficiency.

Cases 9, 26, 36, and VII are especially interesting as showing what remarkable variations may occur in one individual under varying circumstances. Thus in Case 9, a colored woman with great cardiac dilatation, the output during a period of decompensation six months before death was 25.6 per cent. Under rest and diuretics there was great improvement, and death came on suddenly while the patient was apparently in fair condition. Twice later, when compensation was reasonably good, sixty-eight and ten days before death respectively, the 'phthalein output was 58.6 and 59 per cent.

In Case 26, a colored man with syphilitic aortitis and aortic insufficiency, the 'phthalein, during a period of decompensation, was 24 per cent.; a week later in compensation it was 63 per cent.

In Case 36, a colored man with fibrous myocarditis and chronic mitral disease while in a condition of grave decompensation five weeks before his death, at a time when the urine was very scanty and showed a trace of albumin and hyaline and granular casts, the 'phthalein output was but a trace. A week later the patient was much better and, although he was still œdematous, the output of urine was above the intake. The 'phthalein excretion was 38 per cent. One day before death when the urine again was very scanty the output of 'phthalein was but a trace.

In Case VII, a man of 61 with myocarditis and dilated heart, the output of 'phthalein six months before death during a period of decompensation was 16 per cent. A week later, when he was improving, it was 36 per cent. Yet a week later it was 48 per cent.

The *urine* in these instances of chronic passive congestion was scanty, the specific gravity normal or increased. There was a trace of albumin and a few casts, excepting in Case 10, where toward the end, in association with a terminal infection, there was from 0.6 to 0.7 per cent. of albumin and numerous hyaline, granular, and epithelial casts. Anatomically, in this instance, there was extensive acute epithelial necrosis, but no 'phthalein test was made at the periods when this must have occurred.

The *blood pressure* in these patients, most of whom showed cardiac hypertrophy as well as dilatation, may be seen in the accompanying table.

BLOOD PRESSURES.

Case 5	160 to 187
Case 9	170 to 210
Case 10	135
Case 12	100 to 122
Case 14	120 to 130
Case 16	82 to 124
Case 19	200
Case 22	175 to 210
Case 25	95 to 124
Case 26	120 to 160
Case 32	180 to 182
Case 35	202 to 242
Case 36	130 to 175
Case 37	150 to 175
Case V.	112 to 150
Case VII.	135 to 150
Case VIII.	125 to 190
Case XI.	135
Case XII.	110
Case XIII.	100 to 115

The figures for our instances of chronic passive congestion show then, in general, a moderate diminution in the amount of 'phthalein excreted in two hours, a diminution which, in some cases, may be extreme, amounting almost to complete suppression. This is wholly in accord with the experiments of Rowntree and Fitz.

In 9 cases (14, 16, 19, 22, 25, 26, VII, VIII, XI) other tests of renal function were carried out, as may be seen in the following table.

TABLE V.—Showing Various Tests of Renal Function in Cases of Chronic Passive Congestion.

No. of cases.	'phthalein excretion in two hours.	KI.	Lactose.	Chlorides.	Grammes of in-coagulable N. per litre of blood.	Grammes of urea per litre of blood.
14	37 per cent.	68 hours.	9 hours.	Retained	0.49	
16	48 per cent.	72 hours.	19 hours.			
19	50 per cent.	56 hours.	10 hours.	Retained	0.21	
19	A week later, improved; polyurea.			Good excretion		
22	35 per cent.	62 hours.	10 hours.	0.4	
22	3 days later.	0.36	
25	71 per cent.	80 hours.	9 hours.	Retained	0.192	
25	55 per cent.	..	12+ hours.	0.47	
26	24 per cent.	48 hours.	Trace only in 1 hour.	0.33	
26	63 per cent.	..	4 hours (normal amount)			
VII	16 per cent.	Poor excretion		
VIII	54 per cent.	48 hours.	50 per cent. in 3 hours.	Good excretion		
VIII	Later	..	Trace only in 5 hours.	Good excretion	0.5
XIII	61 per cent.	..	Trace only in 4 hours.	0.4	

These tests show the variability of the results with iodide of potassium, on which we have learned to place little reliance. The lactose excretion is profoundly modified in chronic passive congestion. A striking example of this is to be seen in Case XIII, where the lactose is almost suppressed while the 'phthalein excretion is fairly good.

Although the incoagulable N. or urea was estimated nine times in 7 cases, and during periods of grave decompensation where the 'phthalein excretion was as low as 24 per cent., in no instance was the urea above 0.5 nor the incoagulable N. above 0.49 per litre.

It is clear then that chronic passive congestion alone may result in a very marked reduction in the 'phthalein output in the first two hours, a reduction which in extreme instances may amount almost to suppression. With the return of compensation, however, the excretion of 'phthalein rapidly regains the normal percentage.

The incoagulable N. in the blood has not been high in any of our cases even at times when the elimination of 'phthalein has been considerably interfered with.

SUMMARY AND CONCLUSIONS. These observations show, in severe chronic nephritis, a uniformly low 'phthalein output which, as a rule, in those instances not interrupted by an acute terminal process, decreases steadily up to the onset of uræmia, and is nearly or wholly

suppressed from a day or two to a month before death. Acute terminal processes which may be unsuspected clinically, are common, and here a sudden diminution in the elimination of 'phthalein may come on in cases where the percentage previously excreted is not so low as to appear menacing.

In not a single instance, and indeed not once in all the studies of the last five years, have we met with a case of severe chronic nephritis¹ with a good 'phthalein elimination.

Chronic passive congestion (cardiac disease) results often in a considerable reduction in the two hours' elimination of 'phthalein. The results are very variable in individual cases. In marked decompensation the 'phthalein output may be reduced to but a trace in two hours; but the excretion is, as a rule, rapidly restored with the reestablishment of circulatory compensation.

These observations are in agreement with the experimental studies of Rowntree and Fitz.

In the few instances of chronic nephritis of moderate extent which are included among our cases the excretion of 'phthalein was uniformly considerably reduced. All of these cases, however, were associated with chronic passive congestion of considerable extent, but the percentage of 'phthalein was lower than might have been expected with an uncomplicated passive congestion.

In one instance of acute nephritis and in one instance of pure amyloid disease the 'phthalein excretion was greatly reduced.

The cloudy swelling observed in acute infections was in some instances, associated with considerable reduction in the 'phthalein output.

These observations then tend to support our previous impression that the phenolsulphonephthalein test of Rowntree and Geraghty is a procedure of considerable diagnostic and prognostic value, especially in the study of chronic nephritis.

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¹ As has been pointed out by Pepper and Austin and Baetjer there is a stage or form of nephritis in which the excretion of 'phthalein is not interfered with. These instances are more or less characteristic in their clinical manifestations and are often roughly classed as "chronic parenchymatous nephritis." Their most striking clinical features are the elective impermeability of the kidney to salt and the resulting tendency to hydrops. With regard to most other tests of function the kidneys appear to react normally, and beyond the dropsy there are sometimes few disturbing symptoms. These are presumably cases with little glomerular involvement. No such instance has come to necropsy in this clinic.

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**A FURTHER REPORT OF THE PATHOLOGIC EVIDENCE OF
THE RELATIONSHIP OF GASTRIC ULCER AND
GASTRIC CARCINOMA.**

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INTRODUCTION. The following report is a continuation of a study of gastric ulcers and cancers first presented to this society in 1909.¹

Between January 1, 1905, and January 1, 1914, tissues were received for examination in the laboratories of the Mayo Clinic from 870 gastric and duodenal cases.² From 705 of these cases the tissue included the site of the primary lesion. Of these, 260 were simple chronic ulcers without histologic evidence of cancer. Most of these ulcers have recently been critically examined by MacCarty.³ Therefore the gross material and sections from only a small number of the ulcers have been examined by us for comparison with those from the cancer cases. The present review has been largely confined to the study of the gross and microscopic tissues from the 445 gastric carcinomas received in the laboratory during the nine years above mentioned. Of these, 399 specimens were resected by the surgeon and 46 were removed at autopsy from cases on most of whom an exploratory or palliative operation had been done.

DATA. The data for the following report is based on (a) the primary pathologic diagnoses made from the examination of the specimen immediately after its removal, in almost all instances, either by one of us (Wilson) or by MacCarty. This examination included in all cases of at all doubtful character a microscopic examination of frozen sections. (b) The review of all photographs of the entire specimens and of microscopic sections taken at the time of the primary pathologic diagnosis. (c) The review of all sections of fixed tissues previously prepared from the cases. (d) From many cases the study of serial paraffin sections recently prepared and

¹ Wilson and MacCarty, *AMER. JOUR. MED. SCI.*, December, 1909, pp. 846-852.

² During the progress of this study a portion of the data with a slightly different and less accurate tentative grouping was presented before the St. Joseph County Medical Society, South Bend, Indiana, and later published in the *Collected Papers from the Mayo Clinic*, 1913.

³ *Arch. Int. Med.*, 1914, vol. xiii, pp. 208-222.

selected to include, wherever possible, a section through the border and base of the ulcerating lesion. (*e*) A study of the clinical data as regards length of period of previous symptoms and as regards subsequent history. This data has been kindly supplied by Drs. Graham and Eusterman.

CLASSIFICATION OF CASES. All cases in which there was suggestive or positive evidence of cancer have been placed in four groups, as follows:

- 1(?). Ulcer with cancer questionable.
1. Ulcer with beginning cancer.
2. Ulcer with advanced cancer.
3. Cancer throughout the lesion.

GROUP 1(?).—Group 1(?) consists of those cases in which a most painstaking study of the sections gave evidence which was only suggestive of early cancer. The interpretation of the histologic pictures would, no doubt, vary with different observers. In general, it



FIG. 1.—Case I. 5-diameter magnification of section from border of ulcer.

may be said that the suspicion of cancer rests upon profuse aberrant proliferation of the gastric epithelium and, in some instances, on suggestions of infiltration of individual cells or groups of cells into the surrounding tissue. Where infiltration can be accurately deter-

mined there should be no question about the presence of cancer. Where it is doubtful, we must express that doubt. Among the cases in this group is the following:

CASE I.—86829. S. H. F., female, aged forty-one years. History of chronic gastric ulcer seven years; more severe for last six months. Wide excision of supposed gastric ulcer July 7, 1913. Pathologic diagnosis, gastric ulcer. In fair condition six and one-half months after operation. (See Figs. 1 to 3.)

The significance of such cases from the clinical standpoint lies in the fact that of the nineteen in our series three patients have subsequently died of gastric cancer. In all of these, practically all of the small gastric ulcer, was examined microscopically and no evidence beyond such as that seen in the above case was found.

The first of these patients, Case II—5957P, P. J. M., was a male, aged fifty-eight years, who for six years had had symptoms of chronic gastric ulcer. On December 3, 1906, a portion of the stomach was removed for a supposed gastric ulcer. Pathologic diagnosis was doubtful cancer on ulcer. Patient lived three years and one month after operation, dying of recurring gastric carcinoma.

The second patient, Case III—A10131, S. J., was a male, aged sixty-three years, giving a history of chronic gastric ulcer covering a period of two years. May 30, 1908, a partial gastrectomy with excision of a perforating gastric ulcer was done. Patient died of recurring gastric carcinoma twelve months later.

The third patient, Case IV—15038, T. G., was a male, aged fifty-nine years, who had had symptoms of chronic gastric ulcer ten years. September 24, 1908, there was a partial resection of the lesser curvature of the stomach for chronic gastric ulcer. Primary pathologic diagnosis of the tissue removed was ulcer. Patient returned two and one-half years later with an inoperable carcinoma of the stomach, from which he died two years and nine months after his first operation.

GROUP 1.—In Group 1 are placed those cases in which the epithelium is not only aberrantly proliferating but also undoubtedly infiltrating the surrounding tissues and yet in which, on the other hand, the base of the ulcer is free of carcinomatous tissue and gives no evidence of ever having contained such. The following cases will serve to illustrate this group:

CASE V.—28092. W. F. S., male, aged fifty-seven years. History of chronic gastric ulcer for three years; carcinoma, one and one-half months. Resection three-fifths of stomach June 3, 1910. Pathologic diagnosis, early cancer on ulcer, glands not involved. Dead in thirty-six months after operation of recurring gastric carcinoma. (See Figs. 4 to 6.)

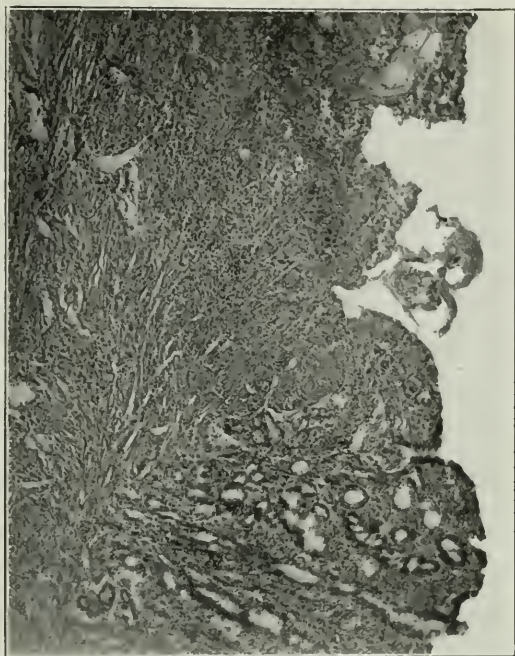


FIG. 2.—Case I. 50-diameter magnification of area marked *B* in Fig. 1.

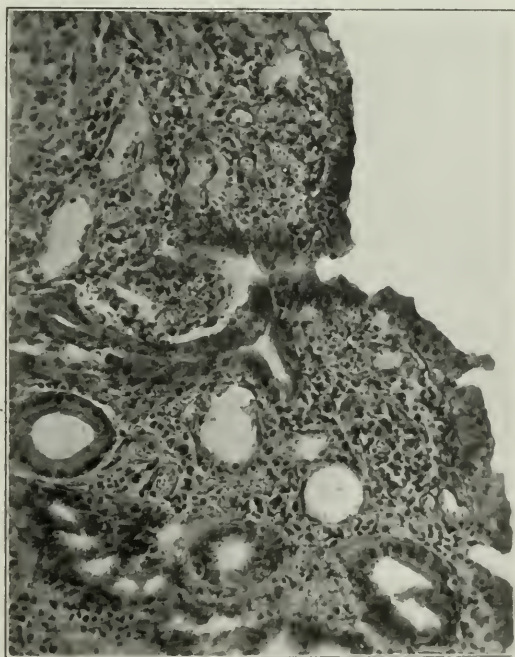


FIG. 3.—Case I. 150-diameter magnification of area selected from Fig. 2, showing markedly proliferating epithelium with doubtful infiltration.



FIG. 4.—Case V. 5-diameter magnification of section from border of ulcer.

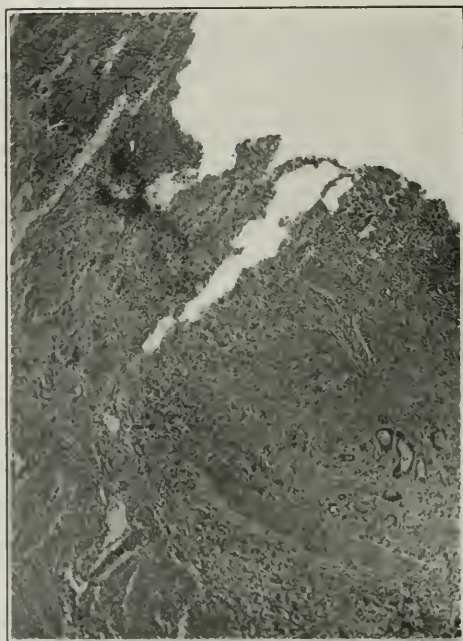


FIG. 5. Case V. 50-diameter magnification of area marked B in Fig. 4.

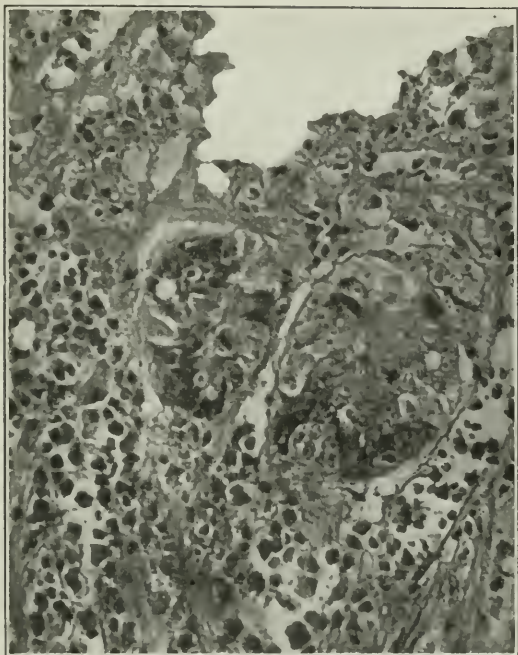


FIG. 6.—Case V. 300-diameter magnification of border area shown in Fig. 5. Note the two groups of cells, the cancerous nature of which is typical though their infiltration is not plain.



FIG. 7.—Case VI. 6-diameter magnification of section across ulcer.

CASE VI.—53784. H. M. S., male, aged forty-five years. History of chronic gastric ulcer for nineteen years. Gastric carcinoma for three months. Resection of two-thirds of stomach June 8, 1911. Primary pathologic diagnosis, early cancer on ulcer; no involvement of glands resected. Patient reported in good condition twenty months after operation. (See Figs. 7 to 9.)

GROUP 2.—The cases included in this group are the cases in which the cancer has more or less invaded the base of the ulcer, and yet in which a well-defined portion of the ulcer remains free of cancer. It is concerning the cases in this group about which most discus-



FIG. 8.—Case VI. 50-diameter magnification of point marked B in Fig. 7.

sion has developed among pathologists, certain observers holding that it is impossible to distinguish in these cases between the development of cancer in the base of an ulcer and the erosion of cancerous tissue forming an ulcer which contains no evidence of epithelium. It seems to us, however, that it is possible in many instances to differentiate between the two conditions, and we have placed in this group only those cases about which we have felt certain that the condition was the former. When a sharp border-line exists between the infiltrating epithelium and the scar tissue and when, at the same



FIG. 9.—Case VI. 600-diameter magnification of group of cells showing early carcinoma selected from area shown in Fig. 8.



FIG. 10.—Case VII. 5-diameter magnification of section through border to base of ulcerated portion.

time, the cancer tissue lies in an antomic plane external to the scar tissue, it would appear that the evidence is preponderatingly in favor of the supposition that the scar tissue existed before the development of the cancer and consists of the remains of the base of a pre-existing gastric ulcer. The following cases will serve to illustrate this group:

CASE VII.—59396. J. D. H., male, aged sixty-five years. History of chronic gastric ulcer for twenty-five years; of gastric carcinoma eleven months. Resection of portion of stomach October 3, 1911. Pathologic diagnosis, cancer on ulcer; three glands on lesser curvature involved. Patient died one month after operation. (See Figs. 10 to 12.)

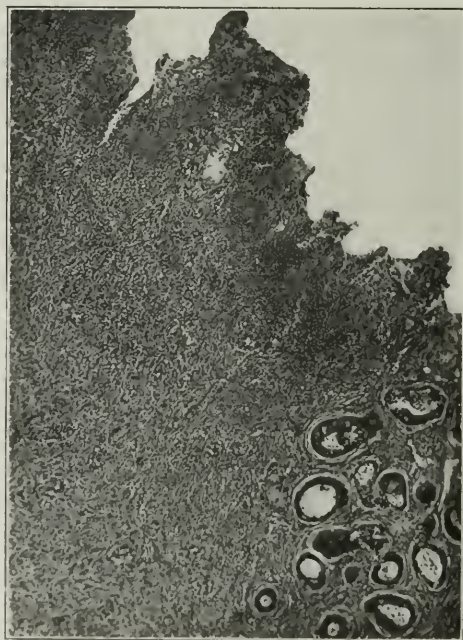


FIG. 11.—Case VII. 50-diameter magnification of area marked *B* in Fig. 10, showing sharp borderline which exists between ulcer and carcinoma in an advanced case.

CASE VIII.—33130. E. W., male, aged thirty-nine years. History of chronic gastric ulcer for many years; of gastric carcinoma one year. Partial gastrectomy January 26, 1910. Pathologic diagnosis, carcinoma on ulcer; one gland in greater curvature involved. (See Figs. 13 to 15.)

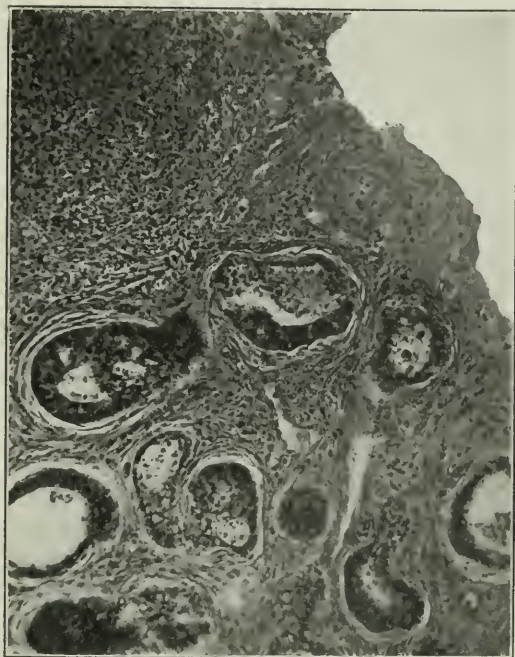


FIG. 12.—Case VII. 150-diameter magnification of carcinomatous area in Fig. 11.



FIG. 13.—Case VIII. 2-diameter magnification of section through base of ulcer.

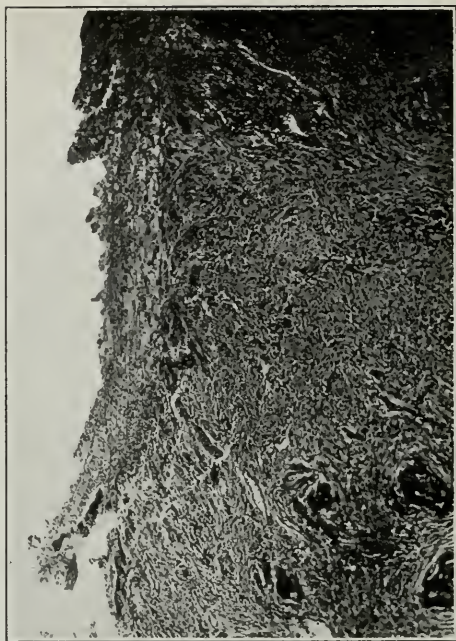


FIG. 14.—Case VIII. 50-diameter magnification of area marked *B* in Fig. 13, showing sharp borderline between ulcer and carcinoma.

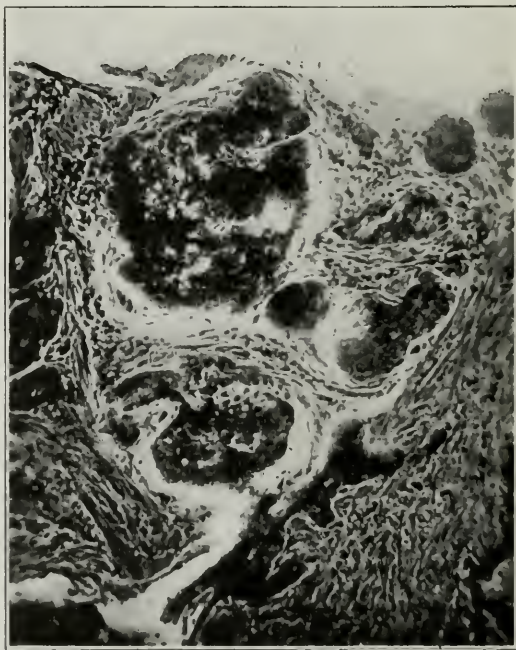


FIG. 15.—Case VIII. 150-diameter magnification of carcinomatous border of section shown in Fig. 11.

CASE IX.—29584. W. C., female, aged forty-nine years. History of chronic gastric ulcer for many years; gastric carcinoma two and a half months. One-half of stomach resected October 8, 1909. Pathologic diagnosis, cancer on ulcer. Patient died of gastric carcinoma six months after operation. Case shown to illustrate that even in advanced gastric carcinoma there may be sometimes found areas in base of ulcer which are free of carcinoma and give no evidence of ever having been invaded. (See Figs. 16 to 18.)



FIG. 16.—Case IX. 2-diameter magnification of section through base of ulcer. Almost the whole of this section, except the area marked *B*, is infiltrated with carcinoma.

These scar-tissue bands extend through to the muscularis. When one studies the structure of the gross specimen in relation to the microscopic section, the impression is very strong that these cancer-free scar-tissue areas are not the result of the destruction of the epithelium as we know does occur in scirrhus cancer elsewhere, but that these masses of scar tissue have been formed prior to the development of the infiltrating epithelium in their neighborhood.

CASE X.—69652. G. E., male, aged forty years. History of chronic gastric ulcer for ten years; gastric carcinoma one month. One-third of pyloric extremity of stomach resected July 1, 1912.

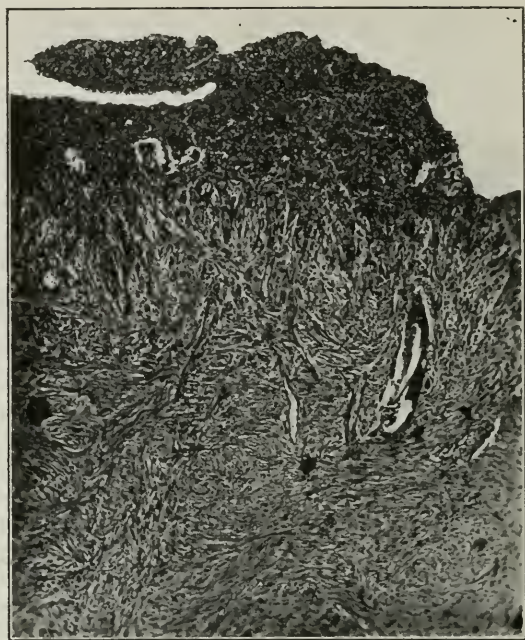


FIG. 17.—Case IX. 50-diameter magnification of area free from cancer shown at *B* in Fig. 16.

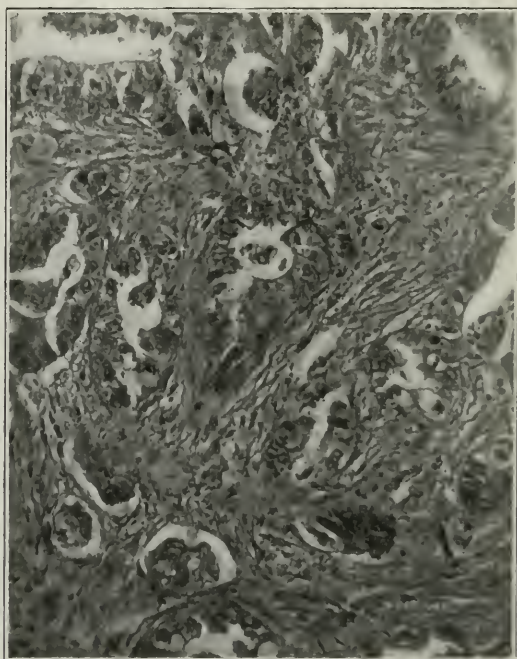


FIG. 18.—Case IX. 100-diameter magnification of area just lateral to that shown in Fig. 17.

Pathologic diagnosis, carcinoma on ulcer. Patient in good condition seven months after operation. (See Figs. 19 to 21.)

GROUP 3. This group contains those cases of cancer in which the evidence of previous ulceration is absent or incomplete. In a very few instances, less than 5 per cent., is the evidence entirely absent. In almost every case in the series there is ulceration, in some portion of which may be found a tract of scar-tissue clear of carcinoma, in many instances penetrating through the muscularis and side by side with areas of cancer which lie in anatomic planes internal to the scar-tissue. Such a condition is seen in the following case:



FIG. 19.—Case X. 4-diameter magnification of section through border and base of ulcer.

CASE XI.—27585. Male, aged sixty-three years. History of chronic gastric ulcer extending over many years. History of cancer extending over a period of three months. Resection of pyloric two-thirds of stomach September 18, 1909. Pathologic diagnosis, carcinoma with extensive glandular involment. Patient died three months after operation. (See Figs. 22 to 24.)

Such a case as this has always been interpreted as ulcerating cancer. However, from the preponderance of cases in which the reverse has been true of the order of development, it would appear



FIG. 20.—Case X. 50-diameter magnification of area marked *B* in Fig. 19, showing line of demarcation between carcinoma and ulcer in base.

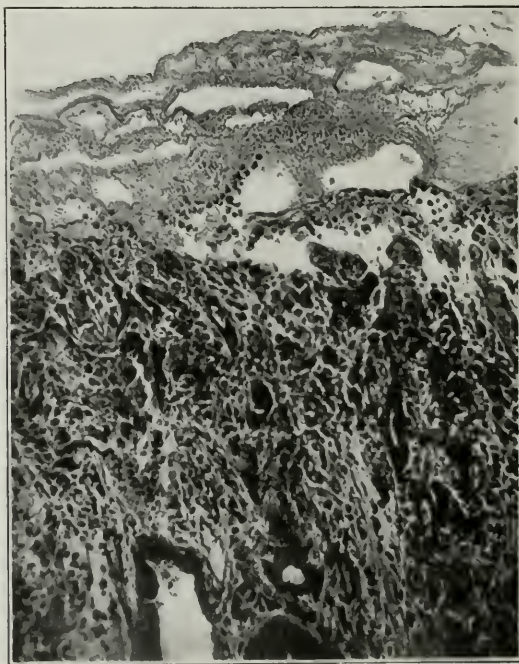


FIG. 21.—Case X. 150-diameter magnification of carcinomatous area as shown in Fig. 20.

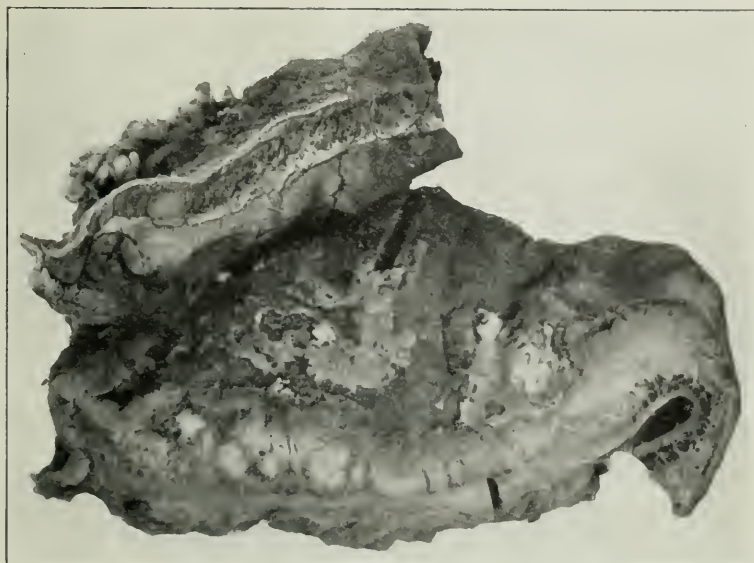


FIG. 22.—Case XI. $\frac{3}{4}$ -diameter magnification of gross specimen, showing extensive involvement of gastric wall.

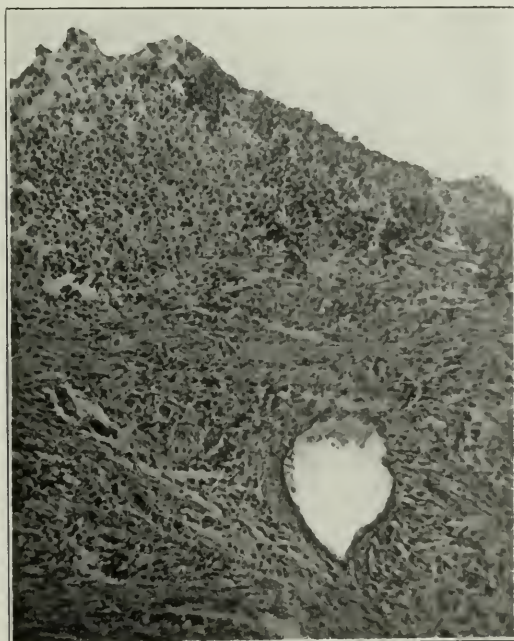


FIG. 23.—Case XI. 50-diameter magnification of area in base of ulcerated portion of stomach. Shows that although the cancer tissue is much scattered it does not extend through to the mucularis and that some portions of the base of the ulcer consist of scar tissue which is cancer-free.

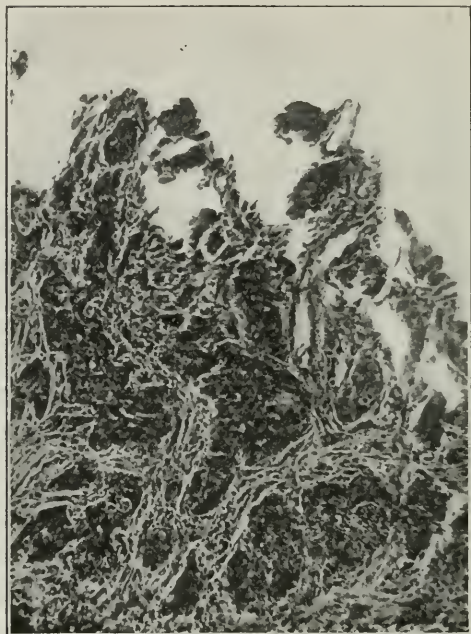


FIG. 24.—Case XI. 150-diameter magnification of cancerous portion of tissue.



FIG. 25.—Case XII. No. 52034. 100-diameter magnification of section from papillomatous cancer of pylorus.

questionable whether we have the right to assume that cases of this kind are illustrations of ulcerated cancer. Indeed, when one considers the clinical evidence in relation to a careful histologic study of a large series of operative cases of gastric cancer, he is led to the opinion that, in all probability, very few cases of gastric cancer exist which have not taken their origin at the site of a previous ulcerative lesion of the mucosa. It is only in rare instances, not more than four or five in our entire series, in which there appears a rapidly growing fungating papillomatous cancer of the pylorus in which no previous ulcerative lesion is suggested. It must be remembered that, even in these, a small chronic ulcer of the pylorus may have been literally covered in by the rapidly growing mucosa. Such a case as this is our Case XII-52034. (See Fig. 25.)

TABLE I.—ANALYSIS OF CASES IN WHICH SPECIMENS INCLUDED THE SITE OF GASTRIC ULCER OR CARCINOMA. CASES OPERATED ON.

	Ulcer	Group 1 (?) Ulcer +Ca?	Group 1 Ulcer + early Ca.	Group 2 Ulcer + Adv. Ca.	Group 3 Ulcer ? + cancer.
Total number . . .	170	19 (4.8%)	63 (15.8%)	147 (36.8%)	170 (42.6%)
Average age at operation	43	51	50	50.9	54.7
Percentage of cases giving chronic history . . .		(58.0%)	(8.5%)	(70.7%)	(48.8%)
Average number of years of chronic history . . .		9.1	9.0	11.1	13.2
Percentage of cases giving severe recent history . .		67.0%	82.5%	89.0%	90.6%
Average number of months of acute history . . .		2.5	4.5	5.0	6.0

Table I contains an analysis of the cases of this series operated on. In the first column are grouped 170 cases of gastric ulcer which are given for purposes of comparison. It will be noted that the average age at operation of these patients was forty-three years, while the average age at operation of the patients with positive ulcer and questionable early or advanced cancer (Groups 1(?), 1, and 2) was approximately fifty years. At the same time the average age of the 170 patients in the tissues of whom there was undoubted cancer with incomplete evidence of previous ulcer (Group 3) was 54.7 years. These clinical data so far as they go, are in harmony with the pathologic findings that gastric ulcer first develops and cancer is implanted thereon, and that, after the latter disease proceeds, it obliterates the evidence of previous ulcer.

When one remembers the numerous instances of advanced gastric cancer which have given no symptoms until within a period of a few weeks prior to death, he is struck with the high percentage of cases between 70 and 80 per cent. (Groups 1(?), 1, and 2) which gave a

history suggesting gastric ulcer and extending over a period averaging from nine years in the early cases to eleven years in the advanced cases. Group 3 shows that only 48.8 per cent. of the cases in which previous ulceration was questionable gave a history of long previous gastric ulcer, though of the cases which did give a history the average period of symptoms was over thirteen years.

Sixty-seven per cent. of the cases of ulcer with questionable carcinoma gave histories suggesting carcinoma extending over an average period of two and a half months; 82.5 per cent. of the cases of ulcer with early carcinoma gave histories suggesting gastric cancer extending over an average period of four and a half months; 89 per cent. of the cases of ulcer with advanced carcinoma (Group 3) gave histories suggestive of cancer extending over an average period of five months; 90.6 per cent. of the cases of cancer with questionable ulcer gave a history suggestive of cancer extending over an average period of six months. These data are interesting in relation to a study of 566 consecutively operated and pathologically demonstrated cases of cancer of the stomach in our Clinic (Smithies⁴).

TABLE II.—ANALYSIS OF CASES IN WHICH SPECIMENS INCLUDED THE SITE OF GASTRIC ULCER OR CARCINOMA. AUTOPSY CASES.

	Ulcer.	Group 1 (?) Ulcer +Ca? 1 (2.2%)	Group 1 Ulcer + early Ca. ...	Group 2 Ulcer + Adv. Ca. 7 (15.2%)	Group 3 Ulcer ? + cancer. 38 (82.6%)
Total number . . .	15				
Average age at operation or autopsy	57.0	...	54.7	54.1
Percentage of cases giving chronic history	50.0%
Average number of years of chronic history	9.0	...	4.0	7.9
Percentage of cases giving severe recent history	76.0%
Average number of months of acute history	1.0	...	2.8	4.5

The analysis of the cases from which the specimens were obtained at autopsy (see Table II) gives little significant data, since the cases are too few. It is worthy of note, however, that the average age at operation of these cases was practically the same in Group 3 as in the cases operated on of Group 3, while the average number of years of precedent ulcer history and the average number of months of cancer history are both shorter than the similar periods for the cases operated on of Group 3. These figures, so far as they go, would suggest that there is a small group of cases of rapidly developing cancer which symptomatically are without evidence of precedent ulcer.

⁴Jour. Amer. Med. Assoc., 1913, lxi, 1792-1799.

TABLE III.—SUMMARY OF SUBSEQUENT HISTORIES (INQUIRIES DATED FEBRUARY 1, 1913)

GROUP 1 (?) ULCER + CARCINOMA (?)	
Total cases reported	5
Alive	1
Condition good	1
Average months after operation	7
Dead	4
Under thirty days	0
Average months after operation	27.5

GROUP 1. ULCER + EARLY CARCINOMA

Total cases reported	41
Alive	23
Condition good	16
Condition fair	6
Condition bad	1
Average months after operation	30
Dead	18
Under thirty days	6
Average months after operation for remaining 12	28

GROUP 2. CANCER ON ULCER. BASE FREE

Total cases reported	94
Alive	35
Condition good	22
Condition fair	4
Condition bad	9
Average months after operation	34
Dead	59
Under thirty days	18
Average months after operation for remaining 41	14

GROUP 3. ULCER? + CARCINOMA

Total cases reported	97
Alive	19
Condition good	12
Condition fair	2
Condition bad	5
Average months after operation	24
Dead	78
Under thirty days	34
Average months after operation for remaining 44	14

The examination of Table III, which contains a summary of the subsequent histories so far as they have been obtained in these cases, shows the following:

Of the 19 patients in Group 1(?), 1 is reported in good condition seven months after operation and 4 are reported dead, an average period of twenty-seven and a half months after operation. One of these patients died of typhoid fever, the other three of cancer.

Of the 41 patients in Group 1 from whom subsequent histories have been received, 23 are reported alive; 16 of these were in good condition, 6 in fair condition, and 1 in bad condition, an average of thirty months after operation; 6 died in less than thirty days after operation, and 12 were reported dead, an average period of twenty-eight months after the operation. So far as we have been able to determine all of these patients died of cancer.

Of the 94 patients in Group 2 of whom subsequent histories have been received, 35 are reported alive, 22 in good condition, 4 in fair condition, and 9 in bad condition, an average of thirty-four months after operation; eighteen of these patients died in less than thirty days after operation and 41 more were reported dead, all except 1 apparently of recurrent cancer in an average period of fourteen months after operation.

Of the 97 patients in Group 3 of whom subsequent histories were received, 19 were reported alive, 12 in good condition, 2 in fair condition, and 5 in bad condition in an average of twenty-four months after operation; 34 died in less than thirty days after operation and 44 others were reported dead on an average of fourteen months after operation. An analytical study of the clinical data on these cases will be presented later by Drs. Graham and Eusterman.

SUMMARY. 1. Of the 399 cases of gastric cancer from which the tissue containing the primary lesion was resected in the Mayo Clinic, 4.8 per cent. show ulcers with doubtful cancer in the border (Group 1(?), 15.8 per cent. show ulcer with positive early cancer in the borders only of the lesion (Group 1), 36.8 per cent. show ulcers with advanced cancer (Group 2), while 42.6 per cent. of the cases show cancer in which the evidence of previous ulcer formation is doubtful (Group 3)

2. Of the 46 cases of gastric cancer from which the tissue containing the primary lesion was obtained at autopsy, 1 case (2.2 per cent.) shows an ulcer with doubtful cancer (Group 1(?), 7 cases (15 per cent.) show ulcer with advanced cancer (Group 2), while in 38 cases (82 per cent.) the evidence of ulcer previous to cancer formation is doubtful.

3. The clinical and pathologic data in relation to the development of gastric cancer or gastric ulcer are in close agreement: (a) with regard to the average age at operation; (b) with regard to the average period of previous history suggestive of ulcer; and (c) with regard to the average number of months of acute history. Such an agreement of data from two independent studies of this series of cases is not accidental.

4. It seems probably from a careful study of the clinical and pathologic evidence of this series of cases that gastric cancer rarely develops except at the site of a previous ulcerative lesion of the mucosa.

STUDIES IN PERNICIOUS ANEMIA.¹

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IN the past few years the interest of pathologists and clinicians has been attracted strongly to the group of hemolytic anemias. Recently through the courtesy of Doctor Hans Eppinger and Doctor A. von Decastello, of Vienna, it was my privilege to see a number of cases of hemolytic splenomegaly and of pernicious anemia, and to study sections of the spleens removed at operation. I have been able to collect thirty-one cases of splenectomy in pernicious anemia, either directly reported or mentioned in discussions on papers read. To these may be added one which Doctor Judell, of San Francisco, has kindly allowed me to report, and one operated upon in my service at the University of California Hospital.

The operation originated in the minds of the two Vienna clinicians independently, both of whom sent cases to operation in March, 1913. Doctor Eppinger's work on the liver and spleen is well known. He is a most enthusiastic believer in the important role of the spleen in the production of hemolytic anemia and hemolytic icterus. He has advocated and has had carried out by Ranzi and Exner splenectomy for the relief of Banti's disease, Hanot's cirrhosis, congenital and acquired hemolytic icterus, splenic vein thrombosis, chronic and acute icterus of uncertain origin, and, lastly, pernicious anemia. He has emphasized in several papers the importance of urobilin in the urine and stools as a measure of pathological hemolysis, and with Charnas has elaborated a method of urobilinogen determination in stools. He has pointed out that the iodine content of blood after removal of cholesterin and cholesterin esters runs fairly parallel to the degree of pathological hemolysis in the body. He has dwelt upon the similarity of the histological picture in spleens from hemolytic icterus and pernicious anemia, and he proposed splenectomy in pernicious anemia largely because of the operative results in congenital and acquired hemolytic icterus, reported by Banti, Micheli, Kahn, Chauffard, and others. He reports five cases from a few days to three, four, seven, and nine months after operation. In all five patients pathological hemolysis was shown by the icteric coloring and large amounts of urobilinogen in the stools. The operation put an end to the increased blood-destruction, and, though Eppinger does not believe that the seat of the disease is in the spleen, he is convinced that "hypersplenism" is an important factor. Three of his patients have returned to business and another is decidedly

¹ Read before the meeting of the Association of American Physicians, at Washington, May, 1914.

better than before the operation. A man operated upon in March I saw in September, 1913. He had gained thirty-six kilograms since the operation and was at business, but his color was not normal and the blood was still of the megalocytic type.

G. Klemperer and Hirschfeld have reported eleven cases operated upon by Mühsam. Three patients died as a direct result of the operation and two shortly afterward. Many cases were in a desperate condition when sent to the surgeon. Here, as in other reports, one is impressed with the temerity of the clinician who refers, for operation, patients with blood-counts of 500,000 to 700,000 and hemoglobin estimations of 10 to 15 per cent. Klemperer had long thought of splenectomy in pernicious anemia for other reasons than those of Eppinger. The first suggestion came from a case of Banti, with marked secondary anemia, that was operated upon by Mühsam and returned after one and a half years with polycythemia. Several instances of polycythemia after removal of the normal spleen or the diseased spleen in Banti's disease are cited from the literature. The theory is advanced of some normal regulating function of the spleen upon the activity of the bone marrow; after removal of the spleen, particularly when diseased, this inhibition is released and normal and abnormal erythrocytes are thrown rapidly into the circulation. In nine cases there were great numbers of normoblasts and erythrocytes with Howell-Jolly bodies in the peripheral blood. In one case seven months after operation megalocytes were prominent in the blood-picture, and there was no difficulty in recognizing the pernicious type. The authors agree that splenectomy may bring about remissions when other means have failed, but Hirschfeld states plainly "*Die Splenektomie bei der perniziösen Anaemie ist nur eine symptomatische palliative Therapie.*"

Von Decastello was influenced in his advocacy of operation by the results obtained by Banti, Micheli, and Antonelli with splenectomy in hemolytic icterus and hemolytic anemia. He reports 6 cases, in 2 of which death followed immediately upon the operation. In a woman, nine months after operation, who improved greatly in strength and for a time in the blood-picture as well, the blood is again slowly changing to the abnormal megalocytic type with high color index. In a second patient the same return of megalocytosis was observed after an initial rapid improvement. In a third case the glossitis described by Hunter first appeared after operation and the blood-picture changed very slowly, and only after four weeks' treatment with arsenic. In a fourth instance improvement was rapid, and six months after operation the blood-count is 4,000,000, with practically normal erythrocytes. Von Decastello notes particularly the cessation of stomach symptoms and the disappearance of profound weakness almost immediately after operation. He records also the persistence of achylia. He assigns some of the benefit after

splenectomy to the increased activity of the bone marrow, and he concludes that in all probability splenectomy will only lead to remissions and not to cure.

Port noted the rapid disappearance of urobilin from the urine after operation and the usual increase of normoblasts and Howell-Jolly bodies. He could demonstrate no hemolysins from alcohol and other extraction of the spleen. Huber's patient, a woman, was not benefited by splenectomy; in fact the blood changed for the worse and large amounts of urobilinogen were still present in the stools. Mosse reports the apparent cure of a woman aged thirty-eight years, four months after operation. The blood-picture is now normal; before the operation it showed 1,100,000 erythrocytes, 3000 leukocytes, and 30 per cent. hemoglobin. He mentions also a case of hemachromatosis, which he includes among the hemolytic anemias, as much benefited after splenectomy.

Türk in his interesting paper, "Die Bedeutung der Milz bei anemischen Zuständen in Bezug auf Pathogenese und Therapie,"² mentions a case three months after splenectomy. The blood-changes were still unmistakably those of pernicious anemia, glossitis and stomatitis had returned worse than before the operation, but had yielded again to arsenical treatment. Pappenheim in the discussion following Türk's paper mentions a case in the Kraus Clinic, Berlin, operated upon three and a half weeks before. The general condition and the blood-picture were both worse, despite the appearance of many Howell-Jolly bodies and other regenerative signs. Roemer³ mentions a patient, a woman, aged fifty-five years, whose blood was once brought nearly to normal by arsenical treatment. She was operated upon during an exacerbation when treatment had failed to give any bone-marrow reaction and with a blood-count of 500,000 and hemoglobin 10 per cent. A tremendous reaction followed operation, with disappearance of poikilocytosis and a rise in count to 1,500,000 and hemoglobin 35 per cent. Improvement continued for four weeks, but was followed by a relapse in the last two weeks. A second case, operated upon fourteen days before, showed improvement, but Roemer is certain that this will not continue.

Harpole and Fox report remarkable improvement in a case sent to operation on account of the failure of other methods of treatment and of the enlarged spleen. There was the usual postoperative normoblastic crisis. They had not heard of the Vienna cases at the time. Von Decastello mentions a verbal report of von Jagie without giving any details of the operated case.

Doctor Judell's patient, a woman, aged fifty-two years, had been ill two years. Mental confusion and vomiting had been prominent symptoms. Splenectomy was done February 23, 1914, largely under local anesthesia, with small amounts of gas and ether. The

² Deutsch. med. Woch., February 19, 1914.

³ Aerztlicher Verein zu Hamburg, February 17, 1914.

blood-count the day of operation showed 2,860,000 red cells and 5160 leukocytes. Immediately after the operation vomiting and abdominal distress ceased. The mental symptoms have grown worse. April 19, 1914, the blood-count was 3,050,000 red cells, 7600 leukocytes, with 31 per cent. polynuclear neutrophils, 66 per cent. lymphocytes, 2 per cent. large mononuclear forms, and 1 per cent. basophiles; 7 normoblasts and 4 megaloblasts were seen during the differential count. In this case there was no active hemolysis before operation, as evidenced by urobilin in urine or stool, and the subsequent marrow reaction was slight, comparatively few normoblasts appeared in the blood, and there were practically no Howell-Jolly bodies.

A man, aged sixty-one years, a native of Sweden, was examined a number of times at the University of California Hospital from April, 1913, to January 26, 1914. He had been weak and unable to work for five years before his first hospital entrance, and probably in those years had had at least two remissions of the disease. There had been moderate nausea and vomiting at different times, and recently some dull, dragging pain in the left hypochondrium. For a month tingling had been felt in the fingers and toes. The yellowish color of his face had been noticed only recently. Sexual power had been absent for four years. The spleen at first was large by percussion and later was plainly felt. A note was made April 15, 1913; "His color suggests a combination of pernicious anemia and chronic heart disease." The sparse hair, thick features, large hands, with chronic joint changes, the small thyroid, the history of impotence suggest a polyglandular syndrome. Achylia was determined on several occasions. The Wassermann, luetin, and von Pirquet tests were negative. Urobilin was increased in the urine and urobilinogen in the stools. The stools were negative for parasites. Glossitis was never present. From May to December, 1913, the patient was at home gradually growing weaker, though there was a slight remission in September. Paresthesia had risen from the feet to the level of the umbilicus and from the hands to the elbows. As there had been no improvement in symptoms or in the blood-picture under treatment with arsenic the patient was referred January 13, 1914, to the surgical service for splenectomy. Urobilin in the urine at this time was moderately increased, urobilinogen in the stools slightly so. Splenectomy was performed January 15 by Doctor W. I. Terry under gas and oxygen and ether anesthesia. The spleen was bound by adhesions to the diaphragm, stomach, and at the lower pole to the omentum. It was freed with difficulty, the operation lasting one hour and forty minutes. The splenic artery was tied before the splenic vein. The weight of the organ was 390 grams. After operation there was marked meteorism and considerable cough. Bronchopneumonia developed in the left lower lobe, gradually progressed, and the patient died January 26 from

bronchopneumonia, thirteen days after operation. There was a recent vegetative endocarditis of the aortic valves. There was no increase of hemolymph glands, while the marrow of the long bones could not be examined. Despite the postoperative infection there was well-marked evidence of an active bone-marrow reaction. Urobilin was not present in the urine after operation. Urobilinogen in the stools was moderately increased January 18, 19, 21, and 23.

Of the 33 cases of splenectomy for pernicious anemia recorded above, 8 died immediately or not long after the operation. There can be no question that in a number of instances rapid improvement followed the surgical procedure. A few patients have regained strength so rapidly—long before the blood-count has risen much—as to confirm the opinion of Banti that poisons from the spleen act at times hyposthenically. A patient of Eppinger's gained greatly in weight. Von Decastello and Doctor Judell have noted the improvement in appetite and the disappearance of stomach symptoms. The achylia persisted in von Decastello's cases. In nearly all instances reported the pathological hyperhemolysis was controlled by splenectomy. The icteric coloring, if present, disappeared, the liver became smaller, urobilinuria ceased in a few days up to two or three weeks, and urobilinogen in the stools was no longer excessive. In the case of Huber, however, urobilinogen was still present in large amounts in the stools three months after operation. In a case of Eppinger's urobilinuria persisted and urobilinogen in the stools was still increased. My patient noted the complete disappearance of the characteristic paresthesia that had been so annoying before operation. Chief interest centres in the remarkable changes in the blood-picture almost immediately after operation, the characteristic feature being the appearance of great numbers of normoblasts, reticulated erythrocytes, and erythrocytes with Howell-Jolly bodies. There can be little question that there is an active marrow reaction. Klemperer speaks of the removal of a hormone that normally inhibits bone-marrow activity; he regards the long persistence of normoblasts and Howell-Jolly bodies after splenectomy in pernicious anemia as evidence of the persistence of some abnormal marrow irritation. Von Decastello suggests that perhaps the marrow reaction is due to the irritation of some abnormal constituents of erythrocytes that have been deprived of the usual modifying influence of the spleen; the remarkable rise in hemoglobin observed in a few instances may indicate an unusual amount of readily elaborated material in liver and marrow. Von Decastello remarks upon the analogy of the blood-changes after splenectomy with those seen occasionally after small blood-transfusions. We have seen above that at times the removal of a normal spleen may be followed by polycythemia by an evidence of hyperactivity of the bone marrow. The normoblastic and Howell-Jolly body crises after splenectomy for other conditions than pernicious anemia are, however, by no means so

marked. Howell-Jolly bodies do not appear after splenectomy in rabbits or mice, but may be observed in great numbers after the operation in rats. Von Decastello and Biedl have seen them after splenectomy in normal dogs. It is interesting to note the constancy of their occurrence in the blood from cases of hemolytic icterus. Schur found them very plentiful in a case of pernicious anemia which at autopsy showed a markedly atrophic and fibrous spleen. The great numbers of normoblasts persist usually for two or three weeks, rarely longer; the nuclei may either be normal or irregular and fragmented. The Howell-Jolly bodies have been much increased as late as seven months after operation; they may occur without much or even any improvement in the general blood-picture. At times there is a quick rise in the number of erythrocytes, 1,000,000 within a week. There may be rapid improvement in anisocytosis, poikilocytosis, and the number of megaloblasts, and the color index may quickly fall. Megalocytes disappear more slowly and the characteristic megalocytic type of blood may be found months after operation when the patient feels quite well or, after initial improvement or even disappearance, the megalocytic picture may be reestablished. Occasionally the red-cell count increases very slowly while the percentage of hemoglobin steadily rises. Von Decastello notes the unusual count of 1,710,000 erythrocytes, 4560 leukocytes, 70 per cent. hemoglobin, and a color index of 2. The leukocytes may or may not increase after operation; usually they do, as after splenectomies in animals. Both Klemperer and v. Decastello mention the polymorphism of the neutrophilic nuclei. This is a common feature of pernicious anemia, but not often described. Doctor Briggs at the University of California Hospital has in 10 out of 12 cases found a marked increase in the number of lobes of the nuclei of the neutrophils, often five to eight—a shift to the right in the terms of Arneth. In 8 cases of severe secondary anemia the number of lobes in the nuclei were either normal or diminished. Usually the blood-plates in pernicious anemia are decidedly diminished, after splenectomy they may be much increased, and at times may form a striking feature of the blood-slide. Fragility of the erythrocytes has been measured in a few cases. In Mosse's case there was decreased resistance to salt solutions, in von Decastello's cases and in a case of mine the limits were essentially normal. Splenectomy does not here seem to increase the resistance of the red cells as it does experimentally, and the decreased hemolysis after operation cannot be referred therefore to the production of hardier generations of erythrocytes.

Clinically in pernicious anemia the spleen is reported usually as not enlarged. Cabot records enlargement in 13 of 110 cases, Billings in 5 of 20 cases, McCrae in 6 of 40, from the Johns Hopkins material. Lyon, in his article in Osler's system, mentions three cases in which a diagnosis of splenic anemia had been made on

account of the great size of the spleen. Hunter records autopsy weights of 570, 330, 300, 390 grams. If the weight of the normal spleen be placed at 150 to 200 grams the organs removed at operation are most often increased in size; 570 (Mosse) 432 (Port), 500, 350, 350, 286, 435 (v. Decastello), 390 (Moffitt).

The spleen is usually described as markedly hyperemic even though the splenic artery has been ligated before the veins; occasionally it may be small, hard, and fibrous. I have had an opportunity of studying sections of the spleen from eight operated cases. The striking thing, as emphasized by all reporters, is the hyperemia of the pulp, the sinuses being comparatively thin and empty. This pulp hyperemia is tremendously marked in the case of Doctor Judell and least marked in my own. The capsule and trabeculae are usually little changed. The follicles may be somewhat atrophied or normal or decidedly increased, as in cases of v. Decastello and in my own. The arteries of the hilus may be sclerotic, tortuous, and even aneurysmal. Eppinger has laid great stress upon certain changes of the smaller arteries which he regards as constant and characteristic. These changes are well illustrated in the following preparations: The walls of the follicular arteries are thickened and the lumen often encroached upon by hyaline masses. The pulp capillaries are also thickened. It is difficult to believe with Eppinger, however, that these vascular changes can divert the normal blood-flow from the pulp and Seidel capillaries to the sinuses and turn it through the intrafollicular capillaries into the interstices of the pulp. As Türk pertinently observes, if the vascular changes were the cause of the pathologically increased hemolysis it is difficult to see how remissions could occur. Occasionally macrophagocytes appear definitely increased and erythrocytes and fragments of erythrocytes can be seen within them. Polynuclear neutrophils can be found in every section, eosinophiles are occasionally seen in considerable numbers, and myelocytes more rarely. In 1 case there were numerous small foci of this myeloid metaplasia. Pigment varies greatly. In 2 cases there was practically none; in 2 there was a small amount of finely granular intracellular pigment, and in 4 there were great quantities of coarse brownish granules in and between the cells of follicles and pulp. The hyperemia of the pulp and the thickened arteries seem to be the constant histological findings, but even these vary considerably in different sections. There is certainly no indication of a greatly increased phagocytic function in any of the preparations.

It is difficult to define the results of splenectomy in pernicious anemia. The removal of spleens with exactly the same histological appearance in cases of congenital hemolytic icterus has led to permanent cure of the disease. In certain cases of pernicious anemia no benefit has been obtained, in others striking improvement has resulted, and cases are reported apparently cured after periods of

three to nine months (Mosse, Eppinger); in still others great betterment in symptoms and blood-pictures has been followed after weeks or months by a relapse. In a few instances threatening exacerbations have been apparently checked by the administration of arsenic. The varying degrees of reaction to the operation must depend upon the condition of other organs, particularly liver, bone marrow, and lymph glands. The role of the spleen in the disease may be compared in part to the role of the thyroid in exophthalmic goitre. Very probably the condition of "hypersplenism" of which Eppinger speaks is brought about by poisons reaching the spleen in the arterial circulation. As in Banti's disease, erythrolysis does not take place in the spleen, but the corpuscles are in some way sensitized and then destroyed in liver, marrow, and lymph glands. The Kupffer cells of the liver have been found in a state of increased phagocytosis of erythrocytes in cases of pernicious anemia, and a number of authors, particularly Warthin, Weigert, and Eppinger, have emphasized the importance and increased activity of the hemolymph glands. After splenectomy in animals large numbers of cells containing erythrocytes are found in the sinuses of lymph glands. Pearce and Austin have noted an increase of endothelial cells in liver capillaries and lymph glands after splenectomy in dogs; these cells become phagocytes of red cells after injection of hemolytic sera and compensate for the erythrocytolysis in the spleen. Pappenheim considers the milk spots of the omentum as rudimentary hemopoietic tissue and thinks they form the "anlage" of multiple splenoid tumors developing after splenectomy which may assume hemolytic functions. Eppinger is inclined to refer relapses after operation to the increased hemolysis occurring in hemolymph glands. He suggests arsenic to check their development, and dwells upon the necessity of early operation in pernicious anemia before other hemolytic organs than the spleen have been involved.

Though since the early work of William Hunter we admit the great importance of the hemolytic function of the spleen, I think we must, with Warthin, realize that the infective agent or toxin of pernicious anemia "may act differently at different times or that there may be several hemolytic poisons, and that there may be splenic, lymphatic, hemolymphatic, or marrow hemolysis." The shifting clinical pictures, the varying reaction at different times to remedial measures, like arsenic, blood-transfusion, thorium X, salvarsan, splenectomy, the marked hemolysis in some cases (urobilinuria, icterus) and its absence in others, the inconstancy of marrow reactions, all speak for a widespread influence of the poison in the economy with maximum effects apparent now in this organ, now in the other.

The importance of the bone-marrow reaction has long been known to clinicians, and is again emphasized by the above-described blood-changes after splenectomy. Few conditions apart from pernicious

anemia are marked by a megalocytic type of blood. In the acquired form of hemolytic icterus the anemia may be extreme. The cases reported by Banti in 1911 and Antonelli in 1912, apparently cured by splenectomy, resembled pernicious anemia very closely. A case recently reported by Giffen from the Mayo clinic "suggests the diagnosis of an atypical pernicious anemia." A few normoblasts and megaloblasts were found in the blood, and after splenectomy "a shower of normoblasts and megaloblasts occurred." The spleen weighed 1640 grams. The fact that the patient is living two and a half years after operation, though weak and anemic, speaks much in favor of a hemolytic anemia other than pernicious. Cases similar to this and Antonelli's have been reported by Parkes-Weber, v. Decastello, Chauffard and Troisier, Gilbert, Chabrol and Bernard. Nearly always in this group the spleen is much larger than in pernicious anemia, and the corpuscular fragility is more frequently increased. Undoubtedly the chief hemolytic agent in this group is the spleen, and its removal may permanently put an end to the disease. Perhaps, as Banti and Warthin first suggested and as Eppinger now affirms, there may be some cases of pernicious anemia in which the hemolytic activity of the spleen overshadows other lesions, and perhaps in these splenectomy may as in other hemolytic anemias lead to permanent improvement or even cure. But the proof of this theory is still inconclusive despite the benefit reported from operation. We still feel that the secondary hemolytic organs, liver, lymph glands, and particularly bone marrow, are involved in the disease as well as the spleen. The changes in the blood after operation suggest, it is true, the removal of some inhibitory influence on the marrow, but that the medullary reaction is a most unusual one is shown by the tremendous numbers of normoblasts and Howell-Jolly bodies.

We have in the operation, as Klemperer and von Decastello point out, a means of bringing about a remission fairly certain when other means have failed. But, as every clinician who has seen many cases of pernicious anemia well knows, it is impossible to say that a patient is in a condition so desperate that no remission can again occur. I have seen a man in coma for three days with hemorrhages from gums, nose, and rectal mucous membranes, a blood-count of 600,000, and have seen this same man back at work for a year after the remission that followed directly this desperate situation. Quinke's case with 143,000 erythrocytes recovered from this exacerbation. Hirschfeld followed a case from 1894 to 1907, death occurring in the ninth relapse. William Hunter demonstrated a patient last summer in London who was still at work thirteen years after the disease was first discovered. Pearce, Krumbhaar, and Musser have demonstrated experimentally the slower blood regeneration in splenectomized dogs. Smaller losses of blood cause a graver anemia in these than in normal dogs and shortly after injection of

hemolytic sera their erythrocytes become less resistant and remain so longer than in normal animals. Port in dealing with the various classes of hemolytic poisons notes that the absence of the spleen is an important factor in causing a persisting corpuscular fragility after injection of hemolytic sera. The absence of the spleen is an important factor in increasing the severity of anemia and in delaying the process of repair.

There are many reasons, therefore, for weighing carefully the question of splenectomy in a given case of pernicious anemia. Eight of thirty-three cases died immediately or soon after the operation. Thrombophlebitis, bronchopneumonia, mental symptoms have been complications in other instances. The patients of Pappenheim, Huber, Roemer were worse or little benefited. In two of v. Decastello's cases initial improvement is being followed by relapse.

Certain passages may be quoted from Banti's discussion on the "Clinical Aspects of Hemolysis:" "The spleen (as for that matter, the other organs also) has not an autochthonous and primitive hemolytic function: it responds in a secondary manner to the agents which do not reside within it. . . . Splenectomy does not, therefore, eradicate the disease—that is, the agents of the disease, whose nature and seat remain entirely unknown to us—but eradicates rather the principal instrument, by means of which these agents become pathogenic." We are yet ignorant of the unknown agents which are brought to the spleen and marrow by the circulation and which are the ultimate cause of the disease pernicious anemia. I have in a previous paper mentioned the similarity of the infective pernicious anemia of horses with the disease in man. I have since had opportunity of examining sections from liver and spleen in equine anemia and of observing changes similar to those in human cases. Mack has described hyperemia of the spleen, increase of pigment, in one case marked thickening of the arteries. Erich Meyer and his assistant Seyderhelen have noted the similarity of both blood-picture and histological changes in equine and human cases. Matthes in an article on *Die Hunterische Glossitis bei perniziöser Anemie* emphasizes the infectious nature of the disease and has observed the occurrence of several cases in one family more than once; in one family three members were affected. His assistant, Hurter, tried inoculations into monkeys with negative results. Since my last report another horse has been injected with blood from a patient with severe pernicious anemia but with negative result. On January 15, 40 c.c. of an emulsion in salt solution of the spleen just removed from a man with pernicious anemia was injected subcutaneously into a third horse. Neither temperature nor blood-counts have changed since then up to May 1. Owing to the difficulty of the operation in horses it seems impossible to try the effect of splenectomy in animals in an active stage of the infection.

ANASTALSIS AND THE SURGICAL THERAPY OF THE COLON.¹

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THE physiology and the surgery of the alimentary canal have become so reciprocally interdependent each alternately correcting the mistakes of the other and showing the way and the need for further research, that it is now idle for either of these branches of medicine to proceed to any conclusions which are not finally and carefully weighed in the scales of the other. Witness the immeasurable effect upon the recent surgery of the stomach by the check of physiology, particularly as regards the subject of so-called drainage and the indications for and against gastro-enterostomy, and, in the immediate present, the interesting reversal of this order of progress in the reconstruction by surgery of many preconceived and erroneous physiological notions regarding the function of the colon.

It is true that the effect of physiological pressure has been very slow in making itself felt, else there would be fewer individuals suffering from needless gastro-enterostomies, made by the "practical" surgeon in the bland assurance, as Walter Cannon says, that the human gut is a "system of rubber tubes conveniently arranged for splicing." The utter truth of this humorous view has long been a reproach to surgery, and the words of this gentle humorist have rightly carried greater weight with American surgeons than all the tomes of his physiological predecessors.

Obedient to the law of reciprocal reaction, it now appears certain that surgery will presently return to physiology, in fair exchange for her correcting influences, certain dominant facts regarding the colon which have hitherto been inaccessible to physiological methods of research. It seems therefore that the long hoped for and elysian prospect of a physiologicocochemical control of all intestinal operations is no longer utopian, but actually at hand. Certain it is

¹ Since writing the above, the authors find that Dr. Horsley, of Richmond, in Jour. Amer. Med. Assoc., August 23, 1913, describes a method of interpolating the ileum, somewhat similar to that described in their article. Lardennois, of Paris (personal communication), in order to preserve the valve, transplants it with a portion of the cecum into the sigmoid.

that the sooner there is complete and cordial coöperation between chemist, physiologist and surgeon, the better for the solution of the bewildering maze of gastro-enterocolonic problems, the very existence of which is only just beginning to be recognized. For no one man can be master of surgical technique and of physiological chemistry as well, and it is progressively evident that the modern surgeon has much to offer his laboratory colleagues in the way of hitherto inaccessible material.

The vicarious assumption of the function of one organ by another in close physiological relationship must be much more common than in usually supposed and it no doubt affords explanation of the question so frequently asked, as, for example, of the removal of an appendix or a gall-bladder, "How does the individual prosper without it?" Doubtless, all the vital functions having long since been taken over by allied organs or perhaps by organs heterologous in morphology if not in function, the loss, by surgical removal of the evident and mechanical functions, such as intermittent storage was not harmful to the economy.

While this compensatory power of the human economy is in many cases facultative, it may, on the other hand, as illustrated by the following case, be congenital in type. Lynch has reported² the amazing instance given to him by Professor Stockard of Cornell, of a human being who reached the age of forty years with only ninety-six inches of intestine from the stomach to the anus. The significant point in this case and which bears particularly upon the compensation problem under consideration was that the lumen of the gut was decreased as shown by actual measurements in almost precise proportion to the decrease in the length. This obviously represents an effort of nature to equalize the rate of absorption, and that this was actually achieved is shown by the fact that the individual never suffered any discomfort; was well nourished, and died of an intercurrent trouble without any suspicion of abnormality ever having been suggested.

An excellent operative illustration of the facultative type is probably to be found in the Author's Case No. 988 in which *gradual* intestinal obstruction from ileocecal valve carcinoma becoming complete, was tolerated for ten days, the toxic signs being minimized, whereas, after two months of re-established function, *acute* obstruction at the same point proved fatal in three days, the toxic signs being so fulminant as to cause suppression of liver function and consequent death.³ Seen in this light, it may well be that such an organ as the colon, for example, may, in certain cases have so outlived its usefulness to the human economy by vicarious transfer of function as to quite justify its removal. Many of the authors' cases

² June meeting of the New York Gastro-enterological Society, 1914.

³ Draper-Schlutz, The Glycronic Function of Liver in Intestinal Obstruction, Jour. Amer. Med. Assoc., September 26, 1914, vol. clxiii, p. 1079-1082.

collectively illustrate this point. No. 180 specifically so, because after ileostomy formed movements showed immediately at the stoma, proving that the ileum previous to obstruction had already assumed one clonic function. That from birth on, it had no function save that of a catch basin as intimated by certain enthusiasts, seems harsh and crude—diametrically at variance with every law and precept of biology.

In studying the author's series of eight ileostomies it is easier to believe in the hypothesis of function transfer from colon to ileum than to presuppose that the colon never had any function save that of storing and distributing toxic material. The gross clinical observations on this series of ileostomies alone will be given, the laboratory studies being reserved for a later paper. In each patient there was a marked gain in weight, the fecal movements from the ileum were always solid and the reaction was always acid. What could offer a more direct reversion of the older teaching of the physiology of the ileum?

Consider this question of colonic therapy from another viewpoint. If the organ has a function vicariously transferred for the time, how can we be certain that after a restitution of normal conditions, there may not properly exist an impulse to restore to the colon whatever functions it may have parted with under stress of weather? Such functional restoration has been noted by Satterlee in studying a large number of cases of water trap stomach. It has been found by him little short of amazing to note the rejuvenation of the function of the gastric mucosa after surgical replacement of the organ, and this is particularly so because no gross morphological change was noted in the mucosa at time of operation.

Potential as these queries necessarily must be, they are given kinetic value by the fact that out of any number of persons undergoing total colonectomy a large proportion will die from the immediate effects of the operation. Whatever the vital function of the organ, it is therefore obviously better to retain it *in situ*, either in whole or, under certain conditions of duodenal dilatation as described by Bloodgood, in part; *provided that suitable provision be made for emptying the organ at its oral extremity*. It seems to the writers as inappropriate to speak of cecal "drainage" as of stomach "drainage," since, as shown by one of them,⁴ as well as by numerous Röntgen-ray observations, no drainage of the stomach occurs from its most dependent part, except when the organ be temporarily paralyzed, as in the dilatation of the last stages of pyloric obstruction, because the *emptying occurs directly in line with the peristaltic waves, and not at right angles to them*.

From a study of a considerable number of cases of chronic colonic constipation, the writers are convinced that there is a well defined

⁴ Draper, Studies Surg. Lab. Columbia, vol. i, 1907.

group in which the constipation is due to preponderance of the anastaltic over the prostatic colonic wave. This is easily shown by the rapid transfer of a bismuth enema from the rectum to the cecum and the return to the rectum of a portion of the mass—some remaining in the cecum—the round trip occupying about six to eight minutes. The haustral segmentations are not affected; the return to the rectum is slower than to the cecum: gradually the bulk of the mass accumulates in that organ, and the reciprocal movement ceases.⁵

If, as we believe, there is this form of anastaltic constipation associated with coloduodenal dilatation and insufficiency of the ascending colon, and which can be easily diagnosed by the Roentgen-ray, it is evidently due to aberrant physiology rather than to faulty morphology, placement, or other mechanical conditions, and must be treated by a physiological rather than morphological method.

Anastalsis is therefore necessarily a most important factor in colonic therapy, for all observers are agreed not only as to the frequent existence of the anastaltic wave throughout the colon but also as to its preponderance over the prostatic wave in the group considered.

It is not yet agreed in what exact per cent. of cases this preponderance occurs, but it is assuredly so large as to constitute the most urgent problem yet to be solved in the operation of ileocolostomy. This is positively demonstrated, not alone by several of the authors' cases, but by the actual postoperative clinical findings of those surgeons who are doing this operation most frequently. Patterson asserts that fully 5 per cent. of ileosigmoidostomies require colectomy at a subsequent date because of the packing and progressive dilatation of the partially excluded and occluded segment. It has been shown by the studies of surgical physiologists⁶ that a totally occluded bowel will fill to bursting with fecoid material in a very short time, and that incomplete exclusion results in the so-called "policeman club" dilatation which if untreated results in terminal perforation.

Now as it is well known, the small gut possesses normally but one; the prostatic wave. Upon this fact is based two of the methods of surgical therapeutics outlined below.

Draper (unpublished studies from the Mayo Laboratory of Surgical Chemistry and Physiology, Rochester, Minn.) has shown that circular segments of ileum may be transplanted into the colon without undergoing any gross morphological change. This has also been demonstrated by others. In each of these instances, however, the transplant was designed to bridge a gap in the sigmoid following resection for malignant growth, the operators making no

⁵ Observations on author's cases by L. T. Le Wald.

⁶ Brown Blake, *Studies on Exclusion*. Studies from the Laboratory of Experimental Surgery, Columbia University, vol. i, 1907.

mention of the possible important physiological therapeusis of this procedure. It is evident, however, that such a ring of ileum would serve to block the colonic anastaltic wave and should prevent the

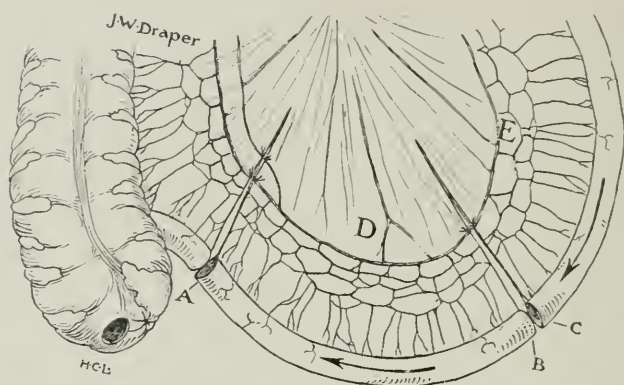


FIG. 1.—Ileo-ceco-sigmoidostomy. A new method of draining the colon with or without short-circuiting. The conditions calling for this physiological method of drainage are severe anastaltic constipation or cecal dilatation, secondary to previous ileo-sigmoidostomy. First stage in technique.

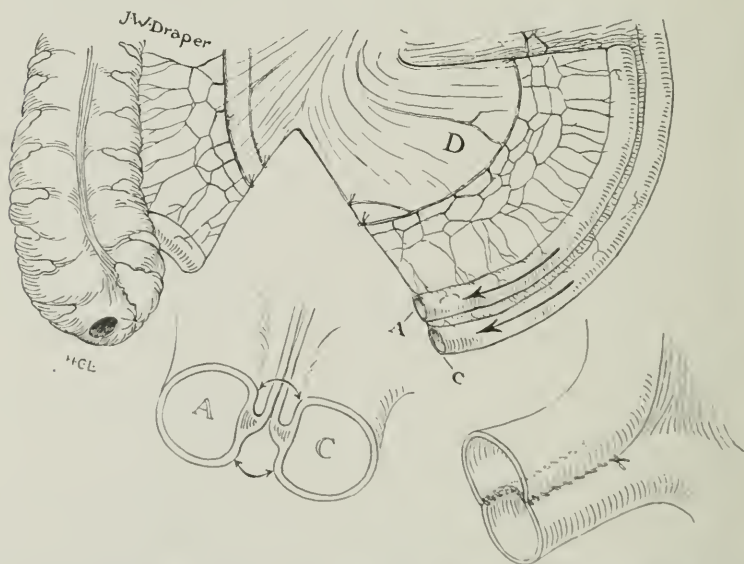


FIG. 2.—Ileo-ceco-sigmoidostomy. Second stage: The ileac segment AB has been slipped cephalad over C. This is done to facilitate the sewing of the ends AC, as shown in the detail sketches.

return of material to the cecum. Halsted was the first to record experimental studies in gut reversal, and we know from his work, and from that of later observers that solid materials have a ten-

tendency to collect at certain points if the course of the waves is broken, and this tendency might or might not be a factor limiting the value of the blocking method suggested.

In the presence of a sufficiently strong wave there might therefore possibly be developed a tapering colonic dilatation immediately aboral to the transplant. This, however, does not occur in the author's experience with this procedure in animals.

The physiological hypothesis which should explain the failure of cecosigmoidostomy may perhaps be found in the fact that the current is distaltic or oscillating. Reasoning from this hypothesis the authors have resorted to the technique shown in Fig. 1, and the work has been done on animals and upon the cadaver.

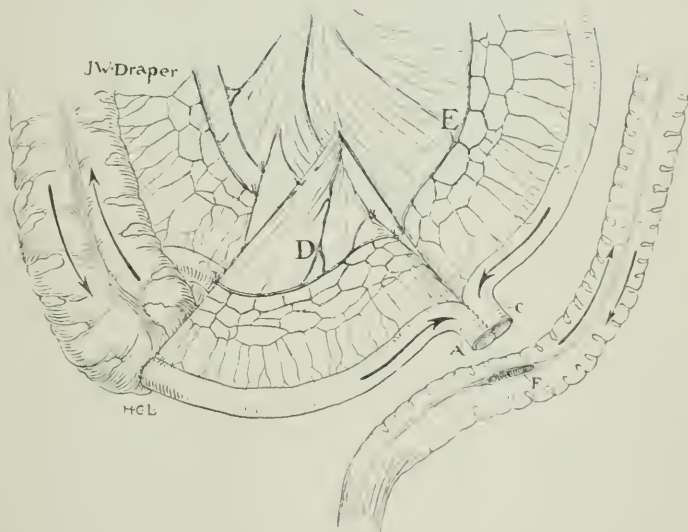


FIG. 3.—Ileo-ceco-sigmoidostomy. The cephalad end of the ileac segment has been united to the cecum and the double-barrel anastomosis with the sigmoid is about to be made. Note the predominant anastaltic wave in sigmoid as shown by arrows.

The ileac segment *B* which is made of proper length to reach comfortably from the cecum to the sigmoid, is slipped up on the ileum and united throughout about half its length as shown. Terminally the aboral ends are sutured together so that a circle results. The effect of this technique is virtually the production of a double-barrel gun, and the end to side implantation into the sigmoid is thus converted into a single procedure. The oral extremity of the segment *B* is then inserted into the oral extremity of the cecum. Material is in this way able to pass from the cecum to the sigmoid, but cannot reverse its direction. The oscillating distaltic wave is made constant or monostaltic.

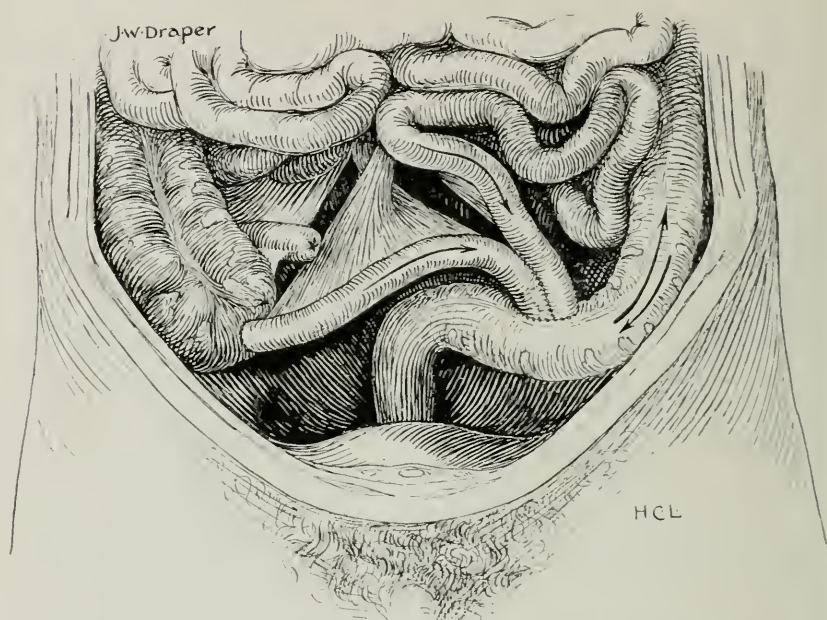


FIG. 4.—Ileo-ceco-sigmoidostomy. The operation is complete, with the exception of closing the ileac fossa.

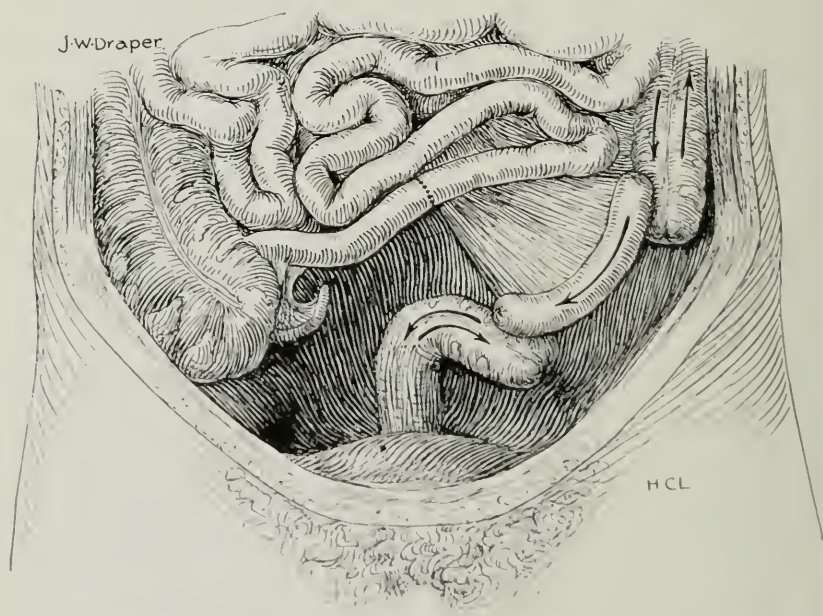


FIG. 5.—Anastaltic block. The monostaltic wave of the ileum is interposed to break the continuity of anastalsis.

Fig. 2 shows the physiological blocking of the anastaltic wave by the transplantation of the prostatic ileac segment. This procedure may be employed as an aid in preventing reflux after the usual operation of ileosigmoidostomy.

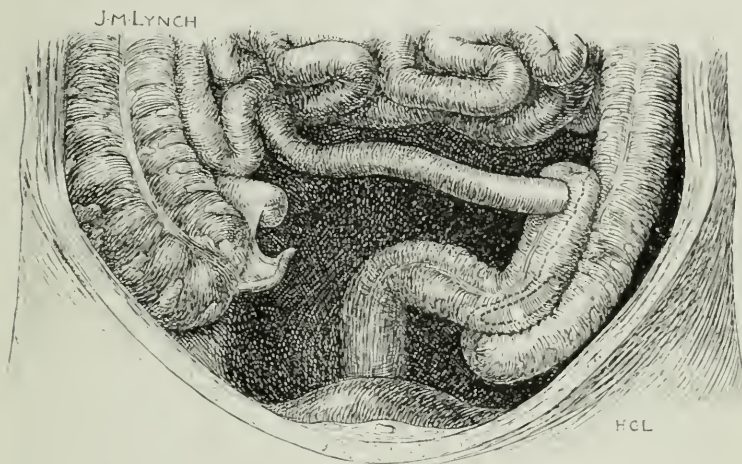


FIG. 6.—Ileo-sigmo-sigmoidostomy. Section and overlapping of sigmoid to block anastalsis. The cephalad current will not pass through the stoma.

Fig. 3 shows a very simple method of preventing anastaltic reflux after ileosigmoidostomy. This operation is performed after the usual technique. After the anastomosis has been completed, the sigmoid is divided between clamps, and by means of a cautery immediately oral to the anastomosis. The aboral end of the sigmoid is invaginated after the usual manner, and the oral end slipped down beside the aboral limb until the oral extremity is several inches below the ileosigmoid anastomosis. The operation is completed by a termino-lateral anastomosis.

THE SUBCUTANEOUS INJECTION OF OXYGEN AS A THERAPEUTIC MEASURE.

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IN 1912 Derosé¹ published an account of a method of injecting oxygen subcutaneously, as being preferable in some cases to the older method of its use by inhalation. It has been the experience of many physicians to finally lose faith in the stimulant and life-saving powers of oxygen, because again and again the appearance of the oxygen tank merely meant that the death of the patient was imminent. Evidently Derosé's announcement created no marked interest, although from time to time notice appeared of the use of the method in a casual way. My own attention was called to the procedure by Dr. Henry O. Howitt, of Guelph, Ontario, who read a paper in July, 1913, at the Canadian Medical Association, upon the results he had obtained by its use. Early in his experience he was so fortunate as to resuscitate a patient whom he thought to be beyond the possibility of recovery, and after a protracted and somewhat disappointing experience of it in hospital practice, a similar result happened in my own work.

Observations appearing in medical literature appear to indicate that the method has been used more in France than elsewhere. In August, 1912, Williams tried the effect of intramammary injection of oxygen gas with an indefinite idea of following the procedure of injecting oxygen into the udders of cows suffering from milk fever. The method was used for the relief of eclampsia, and, reading the author's description, one concludes that the injection was largely into the tissues of the breast rather than into the ducts. Good effects were obtained which the author himself attributes as much to the absorption of oxygen in a general way from the tissues as to any specific effect upon the eclamptic state. Bayeux² treated pulmonary tuberculosis and its consequent breathlessness by a series of injections—twenty in three months—of oxygen into the tissues, with the result that he has a decided predilection in favor of its use. Delmas and Delmas³ detail their experience of its use in the resuscitation of asphyxiated newborn infants, using the gas produced from the action of water on sodium peroxide. The gas was injected into the breast until a lump the size of an orange was raised, and the results were good.

¹ The Subcutaneous Injection of Oxygen; Its Indications, Technique, and Results, Med. Press and Circ. London, 1912, n. s., xciii, 459.

² Traitement de la tuberculose pulmonaire par les injections hypodermiques de gaz oxygène, Ann. de méd. et chir. inf., Paris, 1912, xvi, 337-344.

³ Sur l'emploi de l'oxygène pur comme traitement de la mort apparente du nouveau-né, Rev. mens. de gynéc., d'obstet. et de pédiat., Paris, 1912, vii, 245.

Derosé's method is to employ a metal cylinder, closed by a heavy metal top, which is clamped down; from the cylinder an opening with a tube permits the oxygen to escape. A gauge at the side allows the eye to estimate the pressure of the gas in the cylinder; a block of sodium peroxide immersed in water supplies the gas, of which it is estimated that 2 liters are supplied from 10 grams of the chemical. The gas runs at a low pressure into the tissues, and the treatment may be continued for a considerable time. Sodium hydroxide is commercially supplied in tins, one tin for each series of injections; holes are punched in the tin immediately before it is immersed in the water.

The method I have used consists in conducting the gas from the usual high-pressure oxygen cylinder in every-day use. To the cylinder is attached the usual valve and wheel by which the escape of the gas is regulated. Rubber tubing, about 1 cm. in diameter, and a small needle completes the equipment. The needles supplied with antitoxin answer very well. The whole is clean, the needle sterilized; tincture of iodine is applied to the skin at any desired part, usually the upper thorax; any part of the body where the skin is lax will do equally well. The needle is placed under the surface of alcohol or sterile water so that the rate of flow may be observed. Just short of a continuous stream of bubbles answers best, although the rate does not appear to be of much moment. The needle is then pushed through the skin and according to the less or greater depth to which it reaches, the oxygen will be seen infiltrating in all directions, or a gradually increasing lump rises. Without being able to measure the amount accurately, the usual procedure is to raise a lump of half the size of a foot-ball, thirty seconds or a minute being sufficient time for this amount. If the needle be withdrawn and the opening stopped by a piece of adhesive plaster, it will be noted that absorption usually occurs quickly, in a few minutes the mass will have disappeared, although for several hours the fingers can detect crepitation over the spot; with the stethoscope loud crackles may be heard for a couple of days. The distending process, even where it has been fairly sudden, has never in my experience excited any comment from the patient upon its painfulness.

Many modifications of this mode were used: with the idea of purifying the oxygen, it was bubbled through water, with the result that air-emphysema followed; a rubber bag filled from time to time from the tank seemed to give no advantage, and sometimes the pressure seemed unnecessarily low when it was employed.

Oxygen was applied in this manner to some 33 patients with different diseases; the striking case alluded to above was that of a man, aged thirty years, who, after resection of a large piece of bowel and new growth, appeared to be dying three hours after operation; the lungs were greatly edematous, respirations sixty to the minute,

very shallow; my own impression was that he would die within a quarter of an hour. He was given four large injections during three hours and lived. Although no alteration was noted for a considerable time in the rate of respiration, his comfort increased from the moment the gas was applied.

In cardiac and renal dyspnea the comfort obtained was usually notable: in one case of cardiac disease, where severe dyspnea was met repeatedly by the use of morphin, we were able for several days to replace the morphin entirely by oxygen.

Eleven cases of pneumonia were repeatedly treated, and the results were extremely disappointing. The respiration rate never decreased by more than six per minute, and the rate often remained unchanged. It is true that comfort was at times increased, and cyanosis sometimes lessened; the course of the disease appeared totally unaffected. Such a result might be predicted, if one bears in mind Peabody's⁴ observation that in pneumococcus bacteriemia, the oxygen-combining power of the blood falls with the progress of the disease. A recent paper dealing with uses of oxygen in tissue mechanism and its relation to respiration, by A. G. Auld⁵ will repay reading.

Without making any claims whatever on behalf of oxygen gas thus administered, it remains to be said that here is an easy method of administration in which there is no waste, and in which presumably the oxygen is used as it is needed by the corpuscles and the tissues; further, in cases where respiration is interfered with or is in abeyance, it may quickly be given, and in as many parts of the body in quick succession as is desired. It seems a desirable addition to the armament of the operating-room as a provision against accidents of anesthesia, the more so as it can be administered by a nurse without interfering with those who are concerned, for the moment, in other active measures.

By way of summary, the following states were proved to be amenable to its use:

1. Accidents from anesthesia.
2. Edema of the lungs, edema of the glottis, and accidental interference with respiration by disease of the upper part of the respiratory tract.
3. Marked dyspnea with defective oxygenation, as in cardiac and renal disease.
4. Asphyxia of infants at birth.
5. Syncope.
6. Electrocution.

⁴ Peabody, The Carbon Dioxide Content of the Blood in Pneumonia, *Jour. Exper. Med.*, 1912, xvi, 701.

⁵ Oxygen Want and the Means of its Relief, *British Med. Jour.*, 1911, i, 1060.

NEW GROWTHS INVOLVING THE TERMINAL BILE AND PANCREATIC DUCTS: THEIR EARLY RECOGNITION BY MEANS OF DUODENAL CONTENT ANALYSES.¹

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THE introduction of methods of obtaining and analyzing duodenal contents, aspirated from the upper part of the small intestine by means of the duodenal tube, has made possible a means of diagnosis hitherto unrecognized.

It is at the present time generally conceded that the chemical investigation of the contents of the duodenum gives definite information of the patency or non-patency of the bile and pancreatic ducts.² It will be my purpose to establish a second premise: that tumors of this region usually completely obstruct one or both of these ducts, also to demonstrate that other pathological conditions do not entirely obstruct these passages.

The natural conclusion from these two premises must necessarily follow, namely, complete absence of bile or pancreatic ferments from the duodenal contents determines the diagnosis of new growth in this region. This paper will attempt to establish from facts, the accuracy of the deduction.

In order more fully to understand the mechanism by which the patency of the bile and pancreatic ducts is obliterated by new growths, it is essential to consider the anatomical relations of these channels to the second portion of the duodenum and then to consider the various points of origin of new growths in this vicinity.

In one-third of all instances the common bile-duct does not traverse the head of the pancreas but runs along the posterior surface of this organ to enter the duodenum separately or in conjunction with the excretory duct of the pancreas. In the other two-thirds of the instances the common bile duct in its terminal portion passes through the substance of the pancreas, from which it emerges, to enter in an oblique direction the wall of the second portion of the duodenum, traversing the thickness of the gut at this point for an area varying from a few millimeters to 1 or 2 cm.

¹ This paper is based upon studies carried on in the wards and pathological laboratory of Mt. Sinai Hospital, New York. The author desires to acknowledge the courtesy and kind spirit of coöperation shown him by the attending physicians and surgeons of the hospital during the course of this investigation.

² The technique of the examination of duodenal contents is fully considered in a paper by the author published in the AMER. JOUR. MED. SCI., 1913, cxix, 393.

The bile duct may now penetrate the intestine and open alone into the duodenum, or, as is more common, it may unite with the pancreatic duct, thus forming a common channel, the ampulla of Vater. This ampulla is only a few millimeters in length and breadth and opens into the lumen of the second part of the duodenum, less often directly or more usually through a small knob of tissue, the papilla of Vater, which projects inwardly from the mucosa of the intestine.

It is thus noted that many variations may occur in the course and method of exit of the common bile duct in its relation to both the pancreatic duct and the duodenum. Letulle and Lorrier³ distinguish the following four common types (see figure):

(a) The ducts unite to form a common ampulla. This is considered the normal arrangement.

(b) The ducts unite while still some distance from the lumen of the intestine and enter the intestine by a small common channel, but without the formation of an ampulla.

(c) The ducts open separately into the intestine without the formation of either ampulla or papilla.

(d) The ducts open separately, but through the formation of a papilla.

Because of the great variability in the course of these ducts and in their relationship to each other it will be readily conceived that the obstructive capacity of a new growth arising in this vicinity will depend in great part upon the anatomical conditions which it finds as well as upon the point from which it arises and the direction in which it grows.

ORIGIN OF NEW GROWTHS IN THIS REGION. We recognize six principal points from which a new growth can originate in this vicinity:

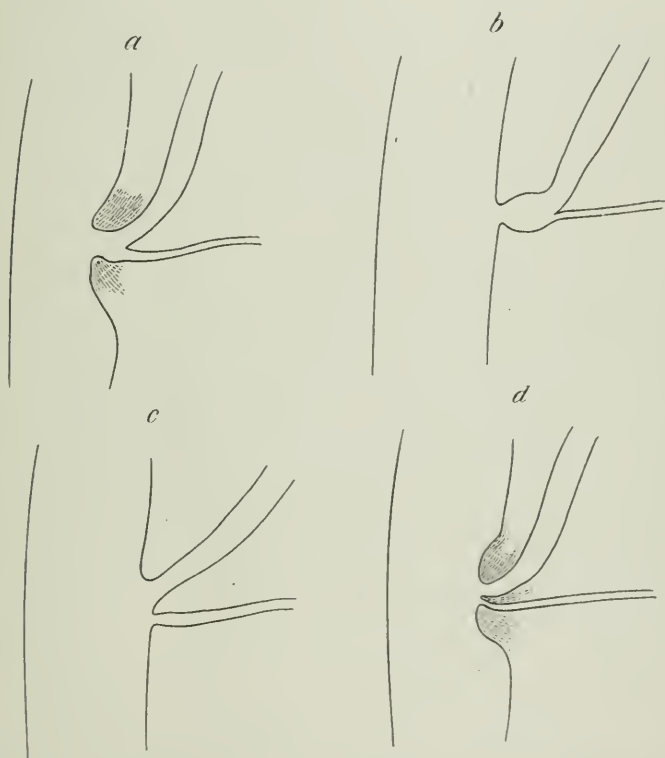
1. The common bile duct.
2. The ampulla of Vater.
3. The duct of Wirsung.
4. The papilla of Vater.
5. The duodenal mucosa.
6. The head of the pancreas.

TYPE 1. *Carcinoma of the Common Bile Duct at or Near its Termination.* This point of origin is fairly frequent as compared with the ampulla of Vater or the duct of Wirsung as a starting-point. One third of all new growths of the bile ducts arise in the lower or terminal portion of the choledochus (Rolleston⁴). Growths originating here are practically always carcinomata. They are small white or pinkish tumors, which early encircle and constrict the lumen of the duct, causing complete obstruction to the passage

³ Quoted from Robson and Cammidge, *The Pancreas, its Surgery and Pathology*, 1907, p. 59.

⁴ *Diseases of the Liver, Gall-bladder, and Bile Ducts*, 1912, p. 691.

of bile. The tumor usually grows along the course of the duct and outward into the duodenal wall, infiltrating the mucosa and finally ulcerating freely into the lumen of the intestine. Once the carcinomatous process reaches the mucous surface of the duodenum it may spread rapidly over this surface as an ulcerating necrosing tumor. Involvement of the duct of Wirsung and the head of the pancreas may also occur.



Diagrammatic representation of variations that may occur in the course and method of exit of the common bile duct in its relation to both the pancreatic ducts and duodenum. (Modified from Robson and Cambridge.)

The duration of this form of carcinoma is five to six months. Local glandular metastases are frequent, involving the lymph nodes on the posterior surface of the head of the pancreas and those in the pancreaticoduodenal angles. The liver may also show a few metastatic nodules. The symptoms are those of gradually increasing and unremitting jaundice, associated with loss of weight and cachexia. In this type of case the gall-bladder is usually firm and globular and distinctly palpable. The stools are acholic.

The clinical picture may be confused by attacks of abdominal colic simulating gall-stone colic, so-called "pseudo-gall-stone colic." Though gall-stones are present in at least one-third of the cases of choledochus carcinomata, yet it is generally recognized that such attacks of pain are due to irritative spasm of the duct, or spasmodic contractions of the tense gall-bladder. The following case is an illustration of the foregoing type:

CASE I.—L. K., female, aged sixty-eight years, was admitted to the service of Dr. J. Rudisch in December, 1913, with the history of gradual appearance of jaundice four months before, associated with sharp cramp-like attacks of pain in the epigastrium, occurring at irregular intervals, frequently at night, and worse after eating. The pains radiated to the right shoulder posteriorly. Vomiting occurred synchronously with the attacks of abdominal cramps. There had been steady loss of appetite and progressive loss of weight.

On physical examination an emaciated woman was seen, deeply jaundiced with a dark olive tint of icterus. The edge of the liver was just palpable at the free border of the ribs. In the region of the gall-bladder an indefinite mass was felt on several occasions, though not constantly. A secondary anemia was present.

The examination of the stool showed blood several times; at first the stool, while acholic, contained no excess of muscle fiber and no neutral fat microscopically. During the progress of the disease both neutral fat and a great excess of muscle fiber appeared.

The duodenal tube was passed on two occasions ten days apart. Both times the contents were milky white in color, slightly acid, and exhibited no trace of bile on chemical examination. The pancreatic ferments were completely absent.

A diagnosis of complete obstruction of both bile and pancreatic ducts by a neoplasm was made.

The patient declined rapidly, evidencing progressive emaciation and unremitting jaundice. Death occurred six and a half months after the onset of the symptoms.

At autopsy (performed by Dr. Wm. Thalhimer) an ulcerated necrosing carcinomatous mass occupied the second portion of the duodenum, overlying and involving the head of the pancreas. The tumor extended upward into the first or descending portion of the duodenum almost to the pylorus.

The common bile duct in its intraduodenal course was laid bare and open by the necrosing mass; the upper end was involved by new-growth tissue, the lower end of the duct was found intact as it entered the preserved papilla of Vater. The duct of Wirsung could not be probed beyond its termination in the papilla, as it soon entered the carcinomatous tissue and its lumen was obliterated. The malignant growth had infiltrated the head of the pancreas;

the body and tail of the gland in addition showed advanced, almost complete fibrous atrophy.

The surface of the liver appeared studded with a few small nodules of new growth; the gall-bladder was slightly distended. Metastatic infiltration occurred in the retropancreatic lymph nodes.

The histology of the tumor was that of a cylindrical-cell adenocarcinoma, such as might arise either from the bile duct or the intestinal mucosa.

The centre of the crater of the tumor, its oldest portion, was located over the terminal portion of the common bile-duct, and this was therefore regarded as the probable point of origin.

In this case the duodenal contents, giving definite knowledge of complete closure of both the large excretory ducts of liver and pancreas made possible a definite diagnosis of neoplasm.

TYPE 2. *Carcinoma Arising in the Ampulla of Vater.* This type of carcinoma is rare, Rolleston,⁵ in 1912, being able to cite only nineteen genuine cases. Hanot,⁶ who has given us one of the clearest descriptions of this variety of cancer, termed it "cancer du pylore pancréaticobiliaire," in contradistinction to neoplasms arising from the duodenal surface of the papilla or from the bile duct. It occurs as a small papillary outgrowth usually limited to cherry size, springing from the inner folds of the mucous membrane lining the ampulla. Such a growth by its mechanical position blocks the two large ducts entering to form the cloaca.

Biliary as well as pancreatic stasis is usually absolute. Secondary inflammatory and obliterative changes in the pancreas occur. Death takes place within nine months from cholemia or emaciation. Secondary growths occur only in the liver, and these in but 20 per cent. of the cases. Histologically these tumors are cylindrical-cell carcinomata.

Of this rarer type I have no examples to offer. Theoretically the duodenal contents in such a case should exhibit absence of both bile and pancreatic ferments.

TYPE 3. *Neoplasms Arising in the Duct of Wirsung.* This is an exceedingly rare form of growth, not more than two or three authenticated cases being on record. It is claimed by Letulle⁷ that these tumors are always spheroidal-cell carcinomata. The case reported by Carnot and Harvier⁸ is a good illustration. The history is that of a woman, aged sixty-one years, who suffered from attacks of pain and vomiting. Ten months later she developed a progressive and intense jaundice, accompanied by advancing emaciation. Death followed an attempt to puncture the distended gall-bladder.

At autopsy a small tumor, the size of a lymph node, occupied

⁵ Loc. cit., p. 703.

⁶ Arch. Gén. de Méd., 1896, ii, 517.

⁷ Presse Médicale, 1906, xiv, 256.

⁸ Bull. et Mém. de Soc. de Méd. d'Hôp. de Paris, 1906, xxiii, 296.

the mouth of the Wirsungian duct at its point of entrance into the ampulla. Complete obstruction of both bile and pancreatic systems was present. The tumor was an adenocarcinoma composed of atypical cuboidal cells. No metastases, either glandular or hepatic, were found.

Of this type of case, with origin in the terminal portion of the duct of Wirsung, I have no example to offer.

TYPE 4. New Growths Arising from the Duodenal Surface of the Papilla of Vater. This point of origin is a more common one, if not the most common, of this group. Of all duodenal carcinomata, 66 per cent. spring from the mucosa of the papilla, forming the so-called "circum-papillary" tumors. Carcinomata arising here are usually cylindrical-cell in structure and histological appearance. They vary in size from a small pea or nut to that of the phalanx of the little finger,⁹ being also described as assuming the magnitude of a small lemon. The form usually taken is that of an excavated or eroded ulcer, depressed in its centre, with raised, overhanging, thickened, carcinomatous walls. The tumor grows by extension into the surrounding tissues, the centre ulcerating the deeper strata while the edge advances. Severe, often fatal hemorrhage frequently results from erosion of larger vessels in the base of the ulcer. In its progress it invades the large excretory ducts in this region, causing obstruction to biliary and pancreatic outflow. Later, as necrosis progresses, these ducts are laid open, thus allowing entrance to infecting bacteria. Suppurative cholangitis and multiple hepatic abscesses are common sequelæ of this type of neoplasm. Metastases occur late in the regional lymph nodes and in the liver, more rarely in the peritoneum and distal organs. The duration of the illness varies from seven to fifteen months, death occurring from icterus gravis, progressive emaciation, hemorrhage, or hepatic infection.

The symptoms are those of obstructive jaundice, associated with diarrhea, melena and emaciation. Rigors and a febrile course are common. The liver is enlarged, the gall-bladder usually palpable. The icterus in this type of case may be intermittent, depending on whether the new growth is in the stage of infiltration and obstruction or in the later stage of necrosis with the release of the withheld secretions. Of this class of carcinomata the following two cases are typical:

CASE II.—D. S., male, aged sixty years, was admitted to the service of Dr. A. G. Gerster May 28, 1913, giving a history of illness of four months' duration, characterized by gradual appearance of jaundice, sour eructations, nausea, and heaviness after meals. The stools had been white since the onset of the jaundice. There had been a loss of weight since the onset of the illness.

⁹ Clermont, *Rev. de Gynéc. et de Chir. Abdominale*, 1913, xx, 33.

On examination the man was seen to be emaciated, deeply icteric; the liver was palpable three fingers' breadth below the free border of the ribs as a smooth, even edge. The gall-bladder was not palpable. Occult blood was present in the stool; the urine was repeatedly negative for sugar. Irregular fever was present.

On operation a mass was felt occupying the head of the pancreas; a cholecystostomy for the relief of jaundice was performed. Death occurred four days later, the patient never having rallied from the shock of the surgical intervention.

At autopsy (performed by Dr. William Thalheimer) an excavated carcinomatous ulcer was noted, occupying what had been the site of the papilla of Vater; the growth was about 2 cm. in diameter, irregularly round, with worm-eaten centre and slightly raised, thickened, carcinomatous rim. Both the common bile and pancreatic ducts were enormously dilated at their termination to the size of an adult little finger; the dilatation of these duct systems extended throughout their entire extent to the capillary origins in liver and pancreas. The terminals of the ducts opened directly into the base of the carcinomatous ulcer, a very fine probe being passable from the duodenal surface into the lumen of the pancreatic duct, but not into that of the bile duct. The duct of Santorini was present, much distended, but ending blindly in the inferior portion of the pancreatic head.

The liver presented two small nodular metastases on its anterior and superior surface. A small lymph node, underlying the head of the pancreas, was infiltrated with new growth.

On microscopic examination the tumor consisted of a cylindrical-cell carcinoma. The pancreas evidenced an advanced interstitial inflammation of the perilobular type. The islands of Langerhans were well preserved throughout.

The duodenal contents of this case, aspirated before the operation, presented a complete absence of bile; pancreatic ferments were present and only very slightly diminished from their normal strength. The diagnosis of complete closure of the bile duct, but patent pancreatic duct, was confirmed by the autopsy findings above quoted.

It is evident that at the time of examination and of death the tumor had advanced to that stage at which carcinomatous infiltration had obstructed the bile duct, but secondary necrosis at its base had allowed a leakage of pancreatic secretion. The enormous dilatation of the entire pancreatic duct system was *prima facie* evidence of previous long-standing occlusion of these excretory channels.

CASE III.—L. J., male, aged forty-eight years, was admitted to the medical service of Dr. N. E. Brill, giving a history of eight days' duration, characterized by constipation and increasing though painless jaundice. On physical examination a moderately

well-nourished man was seen, with a jaundice of a light saffron hue. On abdominal palpation no masses were felt; the liver extended to one finger below the free border of the ribs. The gall-bladder was not palpable. The temperature was slightly elevated during the first two weeks in the hospital, then becoming normal. Blood-count: leukocytes, 6400; polymorphonuclears, 59 per cent.; lymphocytes, 31 per cent.; eosinophiles, 9 per cent. to 12 per cent. Urine repeatedly negative for sugar. The stools were dark brown and large, free fat and muscle fiber being absent; blood was chemically present.

The course of the patient during this time was one of gradual improvement, the jaundice slowly clearing up, temperature becoming normal, and general condition improving. The patient was discharged, twenty-five days after admission, practically well.

Seven weeks later he was readmitted to the hospital, stating that he had remained free of symptoms until four weeks before, when the jaundice had reappeared. His stools had become yellowish white and urine dark brown. He now stated that he suffered from occasional attacks of epigastric pain. On physical examination the liver was felt three fingers below the free border of the ribs, and was tender. The gall-bladder was palpable as a small globular mass. During the four days that elapsed before the operation the temperature assumed a distinctly septic curve, reaching 104° to 105° F. in the evening and approaching normal during the morning.

At operation a small mass was noted occupying the head of the pancreas; the liver was much enlarged and studded with abscesses; the gall-bladder was distended. Cholecystostomy was performed. Death occurred on the succeeding day from shock.

At autopsy (performed by Dr. Olitzky) the site of the papilla of Vater was replaced by an irregularly circular carcinomatous ulcer, 2.5 cm. in diameter. The centre appeared depressed, uneven, and covered with irregular linear depressions and ridges. The edges were thickened and overhanging, composed of pinkish, firm tissue. The choledochus and Wirsungian duct both entered the base of the ulcer, being much dilated throughout their extent. The bile duct was completely closed off by the infiltrating tumor; the pancreatic duct allowed the passage of a fine probe.

The liver was much enlarged, and riddled with smaller and larger abscesses containing thick mucoid pus. The hepatic ducts and their radicles were enormously dilated.

The pancreas was slightly firmer than normal. On the posterior surface of the head was an enlarged lymph node infiltrated with carcinoma, also a similar node in the superior pancreaticoduodenal angle. No other metastases were present in the body.

Histologically the tumor was an adenocarcinoma composed of cylindrical cells. The pancreas showed considerable atrophy of

the parenchyma; the islands of Langerhans were retained throughout.

Duodenal contents obtained from this patient on his first stay in the hospital showed an abundance of thick mucoid bile and very active pancreatic ferments. Reëxamination of duodenal contents after his return to the hospital presented a complete absence of bile; pancreatic ferments were present, though distinctly weaker than on the previous examination.

It is evident in this case that at the time of the first examination with the duodenal tube (two weeks after the onset of symptoms) the growth, then in an early stage, had obstructed the bile duct, causing the jaundice, but already partial necrosis of the tumor had reopened the mouth of both ducts. The jaundice at this date was disappearing.

At the later examination the growth had progressed, completely closing off the bile duct in its advancing infiltrating border, but ulcerating in its centre and allowing the escape of pancreatic secretions. The diminution in the strength of the ferments gave evidence of increasing damage to the pancreatic tissue. At autopsy the enormous dilatation of the two drainage systems offered proof of long-standing and probably complete obstruction for a variable period, followed by necrosis over the mouth of the Wirsungian duct.

TYPE 5. New Growths Arising from the Duodenal Mucosa. This group includes only those neoplasms arising from the mucous membrane of the duodenum, exclusive of those arising from the papilla of Vater, the so-called "circum-papillary" tumors described as Type 4.

Carcinomata of the duodenum are rare, forming only 2.3 per cent. of all intestinal cancers or 0.3 per cent. of all cancers (N. E. Brill¹⁰). According to Rolleston,¹¹ three-quarters of the carcinomata of the small intestine occur in the duodenum. Of 36 cases of duodenal cancers, 8 occurred in the first portion alone (juxtapyloric), 24 in the second portion (including "papillary" cases), and 4 in the third portion alone (infrapapillary).

Carcinomata arising in the mucosa of any part of the duodenum may increase in size by extension so as to involve the papilla of Vater or the openings of the large ducts, and so may simulate carcinomata of the papilla or pancreas head.¹² These tumors are cylindrical-cell adenocarcinomata in type and behave essentially like those of papillary origin. They necrose freely, and in so doing may secondarily release the restrained contents of the ducts.

¹⁰ AMER. JOUR. MED. SCI., 1904, cxxviii, 824.

¹¹ Lancet, 1901, April 20, 1121.

¹² In a case reported by Brill (Mt. Sinai Hospital Reports, 1903, iii, 49), the bile duct at autopsy was opened through secondary ulceration; the Wirsungian duct was caught and closed by the tumor.

Sarcoma of the duodenum is rare, Libman,¹³ in 1900, being able to collect from the literature on the subject only 15 cases. They are characterized by a diffuse infiltration of the walls of the duodenum, dilatation rather than constriction of the intestinal lumen, ulceration, and hemorrhage. Extension into the pancreas and other contiguous organs is common.

The following case, reported in full by Brill,¹⁴ is given here in abstract as a study of this type:

CASE IV.—A. F., male aged eighteen years, suffering for three and one-half years with attacks of sharp epigastric cramps, vomiting of greenish material, and constipation. Attacks continued until six months ago, when he was operated upon and the vermiform appendix removed. He was told that he had cholangitis. The attacks soon recurred after his operation, being characterized by epigastric pain, eructations, and pyrosis. Four months ago he became jaundiced. The bowels moved four to five times daily. He had chills and fever every day, and lost twenty-seven pounds in weight.

Physical examination showed a drowsy, pale, markedly jaundiced boy. There was general glandular enlargement; the liver was not palpable, nor was the gall-bladder palpable.

Blood examination: hemoglobin, 22 per cent.; red blood cells, 1,500,000; white blood cells, 13,000; polymorphonuclears, 85 per cent.

The stool contained blood, but no free fat or excess of muscle fibers. The febrile course was irregular, there being daily afternoon rises. After three months of progressively increasing anemia and emaciation the patient died.

At autopsy (performed by Dr. E. Libman) a friable, necrotic, round-cell sarcomatous mass was found infiltrating the duodenum and extending into the head of the pancreas. The pancreatic and bile-duct systems showed enormous dilatation; the sarcomatous mass had invaded and infiltrated the mouth of both ducts, but the new-growth tissue was of such a soft, friable nature and ulceration had so progressed as to allow of the later seepage of the contents of these ducts through the tumor.

The duodenal contents were obtained from this case on three occasions at intervals of one month. On the first occasion there was complete absence of both bile and pancreatic ferments. This was the stage of obstruction. One month later there was still complete absence of bile, but traces of pancreatic ferments were present. Again one month later traces of bile were present, and also pancreatic ferments in quite normal strength. The earlier complete obstruction had given way, through necrosis of the mass

¹³ AMER. JOUR. MED. SCI., 1900, cxx, 309.

¹⁴ New York State Jour. of Med., 1912, xii, 449.

to more or less free leakage of the pancreatic and biliary secretions into the duodenum.

TYPE 6. *New Growths Arising in the Head of the Pancreas.* Primary carcinomata of the head of the pancreas occur fairly often. It is impossible to estimate from the accumulated literature of years the relative frequency of primary pancreatic tumors as compared with those arising in the large ducts or in the papilla of Vater, for, except in the most recent literature, these various types were all described under the general heading of "carcinomata of the head of the pancreas." Pitt¹⁵ quotes Biash's figures for the frequency of pancreatic carcinoma as 0.12 per cent. in comparison with 0.30 per cent. for duodenal carcinomata; new growths arising in the common bile and pancreatic ducts are relatively much rarer than either of these types.

Carcinomata arising in the head of the pancreas are classically described by Bard and Pic;¹⁶ these tumors are usually spheroidal-cell or cuboidal-cell neoplasms, occasionally colloidal. They grow slowly in the head of the gland, sooner or later involving the duct systems that traverse the organ, to obstruct them. They advance by contiguity infiltrating the surrounding tissues and organs.

The clinical symptoms are those of gastric disorder (nausea and vomiting), attacks of epigastric pain, emaciation, and weakness. When the ducts are involved, obstructive jaundice and fatty diarrhea supervene. Secondary infiltration of the duodenum, when it occurs, creates great difficulty in differentiating these tumors from primary duodenal growths. Metastatic deposits in distal organs are common and take place comparatively early in the course.

The following two cases are typical instances of moderately advanced pancreatic growths:

CASE V.—T. L., male, aged fifty-one years, admitted to the service of Dr. H. Lilienthal, for two and one-half months complained of epigastric pain radiating to the back, griping in character. He had frequently vomited two hours after eating. During the last three weeks he had become jaundiced. There had been marked loss of weight. Physical examination was negative except for jaundice and emaciation.

On operation an enlarged gall-bladder was noted; a stony, hard, carcinomatous mass occupied the head of the pancreas. Cholecystostomy was performed.

The duodenal contents before operation showed faint traces of bile; pancreatic ferments were normally present. Two months after operation, duodenal contents were again aspirated. On

¹⁵ Allbutt and Rolleston's System of Medicine, 1910, vol iv, Part I, p. 303.

¹⁶ Rev. de Méd., 1888, viii, 257.

this occasion no bile was obtained, but pancreatic ferments were again present and quite within normal limits of strength.

It is quite probable that at this point the pathological process had advanced so as to infiltrate and obstruct the bile duct.¹⁷ This patient died eight months later after the typical course of carcinomatous emaciation and cachexia.

CASE VI.—P. V., male, aged sixty-seven years, was admitted to the service of Dr. A. V. Moschcowitz May 22, 1914, giving the following history: Two years ago he suddenly suffered abdominal pains, of a cramp-like nature, localized in the right hypochondrium and radiating to the right and posteriorly to the back. After a few days of severe pain relief was felt. No jaundice was noted.

Six months ago he again experienced sudden abdominal pain about the umbilicus, lasting only a few hours. Since then he had been free of pain, but had noticed a gradually increasing degree of jaundice, with itching of the skin and pale motions. His urine was correspondingly dark. He lost a few pounds in weight.

On physical examination a deeply icteric, poorly nourished man was noted. The most essential points in his examination were the presence of a smooth, palpable liver, the anterior border of which extended to one finger below the free border of the ribs; also a mass attached to the under surface of the liver and moving freely with it. A secondary anemia of a mild grade was present.

The test meal, an Ewald test breakfast, showed complete absence of gastric acid, both free and combined. There was no blood present. The bleeding time of the patient was one and one-half minutes; coagulation time of the blood, four minutes.

At operation a markedly distended gall-bladder immediately became visible. This was emptied by aspiration of over 200 c.c. of dark, viscid bile. No gall-stones were felt. The pancreas was infiltrated and hard, and suggested to the touch new growth; a palliative cholecystoduodenostomy was hastily performed for the relief of the intense jaundice and pruritus. The patient died on the succeeding day of shock and hemorrhage.

At autopsy (performed by Dr. Aschner) a normal sized though firm pancreas was seen to surround completely and to compress the common bile duct in its terminal portion. The duct traversed the head of the pancreas, opening alongside but independently of the duct of Wirsung by means of a well-formed papilla of Vater. The choledochus could not be probed from the duodenal end, resistance being encountered within 0.5 cm. of the intestinal opening. On incising the choledochus it was seen that for a distance of 1.5 cm. the lumen of the duct was completely closed by the inward

¹⁷On many other occasions on which duodenal contents had been aspirated from patients with cholecystostomy drainage, bile was aspirated in large quantities when the bile duct was shown to be open, and none was obtained where permanent obstructive processes existed.

pressure of pancreatic tissue. Above this point the choledochus was enormously dilated, the dilatation of the biliary duct system extending upward throughout all its subdivisions and into the liver. The liver was enlarged and the ducts distended; no new growth was present. The pancreatic duct was not dilated; it was patent throughout.

The pancreatic tissue was firm and hard and exhibited numerous small cysts throughout its extent, these cysts being pea sized and containing thick, clear mucus. Two enlarged soft lymph nodes were removed from the posterior surface of the gland.

Histological examination (performed by Dr. George Baehr) demonstrated a diffuse colloid carcinoma with cyst formation, occupying the entire pancreas; associated with the new growth was an advanced interstitial and intra-acinar pancreatitis. The lymph nodes contained colloid-carcinoma.

In this case the duodenal contents were aspirated on two occasions before the operation. Each time there was a complete absence of bile; on both occasions the pancreatic ferments were present, though distinctly weak.

From these findings it was argued that we were dealing with a carcinoma in or about the common duct in the head of the pancreas; the marked diminution in the strength of the pancreatic ferments suggested strongly either a chronic pancreatitis or a complete disorganization of the pancreas by an extending neoplasm. Both deductions were correct, and were supported by the autopsy findings.

REMARKS. A survey of the preceding types of cases, with reference particularly to the duodenal content analysis of each class, brings forth the following deductions:

TYPE 1. *Carcinomata of the Common Bile Duct.* These cases cause early and complete obstruction of the bile system; in their later extension they may, and frequently do, involve in addition the Wirsungian duct, and completely obstruct it. In Case 1, quoted, the diagnosis was made upon the complete absence of bile and ferments from the duodenal contents.

TYPES 2 AND 3. *Carcinomata of the Ampulla of Vater and of the Duct of Wirsung Near the Ampulla of Vater.* These cause complete obstruction to both of the main duct systems. No original cases with duodenal content studies are quoted. It is probable that both bile and ferments would be absent in these rare cases.

TYPE 4. *Carcinoma of the Duodenal Surface of the Papilla of Vater.* This is a more common type and progresses through two phases: an earlier one of obstruction to the ducts and a later one of necrosis and ulceration with secondary release of the dammed-up contents. It is evident that the duodenal content findings will vary with the stage of advancement of the lesion. In Case II, quoted, bile was absent but pancreatic ferments present; in Case

III, on first examination, both bile and ferments were present (the patient's jaundice was disappearing; evidently necrosis of the tumor had just relieved the ducts). The second examination, weeks later, showed the bile duct completely obstructed but the pancreatic duct still open. The autopsy confirmed these findings.

TYPE 5. *Neoplasms of the Duodenal Mucosa*. These usually grow rapidly and enmesh the mouth of the ducts to obstruct them. A sarcoma (Case IV) is given as an example. The duodenal contents showed absence of both secretions; later examination evidenced some pancreatic ferments and traces of bile leaking through.

TYPE 6. *Carcinomata of the head of the pancreas* frequently avoid the ducts early, but later infiltrate them. Case V is such an illustration, the first analysis of duodenal contents showing both ducts patent, the second examination, obstruction of the bile duct, but Wirsungian duct still patent. Case VI is a similar illustration of this point.

From this summary one fact, at least, seems evident: that new growths in this region usually obstruct one or both ducts completely at some stage of their existence, and that such obstruction is demonstrable with the duodenal tube. Clinically it is not possible to differentiate the various kinds of carcinoma that invade this area. An early and definite diagnosis of new growth versus an impacted stone or obstruction from other cause would be a distinct advantage in that it would make possible immediate surgical intervention.

Complete obstruction of both the main ducts, as evidenced by the duodenal pump, is caused only by neoplasms. Cases I and IV are examples of this point, and the following two illustrations further support the deduction:

CASE VII.—Referred (by Dr. Walter M. Brickner) for duodenal content examination. Mrs. D., aged sixty-two years, noted during the last two weeks increasing painless jaundice, pale-colored motions, and weakness. Physical examination showed an extremely obese woman, markedly icteric. Neither the liver nor the gall-bladder could be felt. The obesity of the patient precluded exact manual palpation.

The duodenal contents showed complete absence of both bile and pancreatic ferments; on this basis a diagnosis of tumor involving the exit of both ducts was made. The patient died after eight months of illness, having developed masses in the liver, ascites requiring tapping, progressive cachexia, and emaciation.

CASE VIII.—Admitted to the service of Dr. Charles A. Elsberg April, 1914. A woman, aged forty-eight years, suffered for three months with absolute jaundice, intense pruritus, and weakness. Bowel movements were large, white, and offensive in odor. She lost twenty-three pounds in weight. Physical examination evidenced a stout, deeply jaundiced woman; on palpation a large mass, thought to be the distended gall-bladder, occupied the right

upper abdominal quadrant. The liver was palpable one finger below the free border of the ribs. Blood was present, chemically, in the stool. The duodenal contents showed blood, but complete absence of bile and ferments. At operation a large carcinomatous mass was felt, infiltrating the head of the pancreas.

Is there any other pathological condition which causes complete closure of both bile and pancreatic ducts? In an experience of three and a half years in the examination of duodenal contents from 102 cases, including 50 cases of obstructive jaundice of doubtful origin, we have met with no instance of this nature except those due to neoplastic obstructions. Complete closure of the pancreatic duct alone has occurred only from tumor formations.¹⁵

The combination of closed bile and open pancreatic duct is commonly observed. Absolute closure of the bile duct is practically always caused by a new growth; in this series of 50 cases with jaundice no other condition but malignancy has been shown to produce absolute biliary stasis, with the following exceptions:

Two cases of stricture of the bile duct following operation upon and direct drainage of this duct (choledochotomy), and one case of chronic intra-acinar and interlobular pancreatitis of advanced degree. In this last case the second examination of duodenal contents showed bile, so that evidently the obstruction was here not really absolute.

Five cases of jaundice due to a stone or stones in the common bile duct presented only partial biliary stasis and no interference with the passage of pancreatic secretions. The statement that stones never cause complete blockage of the common bile duct may appear too sweeping to the view of some surgeons who have experienced large stones firmly impacted in the choledochus near the ampulla, and apparently completely blocking its lumen. Yet the duodenal findings seem clearly to point to the fact that stones do not completely block this duct while neoplasms usually do.

This fact is not a new one, though not usually recognized. For many years it has been known that stercobilin (hydrobilirubin) in the stool speaks in favor of stone obstruction, its absence in favor of neoplasm.

Courvoisier's law, of the enlargement of the gall-bladder to a palpable mass in new-growth obstruction and its failure to do so in stone, is known to be correct in 80 per cent. to 90 per cent. of

¹⁵ The question has often occurred, "Will not the accessory duct of Santorini allow the free entrance of pancreatic ferments into the duodenum where a new growth is blocking the Wirsungian duct?" If the accessory duct were present and patent a false idea might be obtained regarding the patency of the main duct. However in four cases of malignant obstruction of the Wirsungian duct in only one instance was the accessory duct found at all, and in this case the duct of Santorini, much dilated, ended blindly in the head of the pancreas. In the other three examples it was either congenitally absent or previously atrophied. It would thus seem that the duct of Santorini is of more anatomical interest than of pathological importance.

the cases only. Cases in which the law fails to hold true are probably those in which the malignant process has ulcerated and allowed a partial escape of bile into the duodenum. In corroboration of this hypothesis the following table is offered:

Case.	Bile duct (duodenal content examination).	* Gall-bladder.
1.	Obstructed.	Palpable.
2.	Not obstructed.	Not palpable.
3. First examination.	Not obstructed.	Not palpable.
Second examination.	Obstructed.	Palpable.
4. First examination.	Obstructed.	Not palpable
Second examination.	Obstructed.	Not palpable
Third examination.	Not obstructed.	Not palpable
6.	Obstructed.	Palpable.
7.	Obstructed.	Palpable.
8.	Obstructed.	Too obese for satisfactory palpation.
9.	Obstructed.	Palpable.

} Patient a very difficult one to palpate.

Association of stone with tumor of the common duct has been noted in only two cases; the symptoms are those of tumor.

Pancreatitis, acute or chronic (six cases), blocks neither duct; the one exception has already been mentioned.

Hypertrophic cirrhosis of the liver leaves the ducts free, with profuse discharge of bile and ferments.

THERAPY. Having established an early diagnosis of new growth, on the basis of duct closure, it is in the direction of the ever-increasing scope of surgery that we must look for escape from a condition otherwise hopeless. Exclusive of carcinoma arising in the head of the pancreas itself, carcinomata of the other five types have this in common: they grow slowly, increase gradually by extension, involve only the regional lymph nodes directly adjacent to the head of the pancreas, and form distal metastases (practically only in the liver) late in their course.

The remarks of Letulle,¹⁹ in 1906, should be quoted in full, as they most succinctly and clearly point the way to the most reasonable management of these cases:

"All observers note the striking contrast between the gravity of the secondary disorders and the minimal volume and relative benignity of the causal lesion, circumscribed as it is to the zone called by Hanot the pancreatic-biliary pylorus. They have all regretted not having called upon modern surgery for an early interference."

Radical operative procedures have been attempted since the year 1900. Twenty-three cases operated upon have been collected by Clermont,²⁰ in 1913, and the names of the surgeons include some of the most illustrious of our times—Czerny, Körte, Riedel, Kraske, Cuneo, Mayo, Halstead, and others. The operations have consisted in the most part in an attempt to remove locally the new growth with or without the surrounding duodenal wall. Cholecyst-enterostomy as part of the operation has often been performed.

¹⁹ Loc. cit.

²⁰ Loc. cit.

Locally, three different procedures have been attempted:²¹

1. Simple Papillectomy. This operation has been carried out in 8 cases, with the following results: death following operation within eleven days, 3; within eight weeks, 1; death from metastases (after eighteen months), 1; alive at time of writing, 3 (one six months, one six and a half years, one one and a half years).

2. Papillectomy with partial excision of the duodenum (10 cases): Died within a few days of hemorrhage or infection, 4; died of metastases (eight months to two and a half years), 5; alive and well two years after operation, 1.

3. Papillectomy with complete resection of duodenum (3 cases): Died within a few days of operation, 2; lived nine months after operation (died from secondary procedure necessitated by cholangitis and hepatic infection), 1.

Several facts are apparent from a review of these figures:

1. The operative mortality is high (43 per cent).

2. Death from metastases is frequent (28.5 per cent); death from subsequent infection and other causes occurs (10 per cent.).

3. Four cases had remained alive, at the time of Clermont's publication, from six months to six and a half years (19.5 per cent.).

In spite of the apparent disproportion between the number of cases that have succumbed and those that have survived, the latter statement outweighs in importance the former, for it embraces in itself the hope of the future. Increasing surgical skill, earlier diagnosis, and a better acquaintance with the pathological processes that occur here undoubtedly will, before long, bring vastly improving and more gratifying results.

Kausch,²² after operating upon three such cases, has suggested and once performed a two-stage operation of the following nature:

First Stage. Preliminary cholecystenterostomy. This operation relieves the jaundice, improves the nutrition of the patient, and helps to overcome the tendency to hemorrhage at the subsequent laparotomy.

Second Stage. Radical excision of tumor, duodenum, and involved head of pancreas; blind closure of upper end of duodenum; implantation of ablated head of pancreas and common bile and pancreatic ducts into lower end of duodenum; gastro-enterostomy.

Cotte²³ had previously suggested this operation, all in one stage, but subsequently modified his views and proposed the same procedure in two stages.

This two-stage operation will in the future probably become the operation of choice. Though a common practice, it is futile for a physician who makes the diagnosis of "cancer of the head of the pancreas" to resign himself and the patient to the attitude of "there is nothing more to be done." He should remember and understand that a large majority of the so-called tumors of the

²¹ The following figures are quoted from Clermont's article published in 1912.

²² Beitr. zur. klin. Chir., 1912, lxxviii, 439. ²³ Rev. de Chir., 1909, xxxix, 1135.

head of the pancreas are really small localized growths of the common bile duct, ampulla, or papilla of Vater. The greatest number of patients suffering from this disease enter the hospital two to three months after the onset of jaundice. The intervening time has usually been spent by the physician in waiting to observe whether a suspected stone will pass or not. This is the period most valuable for the patient. The proper procedure to follow in a person over middle age who becomes deeply jaundiced, whether painlessly or not, is to attempt immediately to discover, by means of the duodenal tube, whether the main ducts in the region suspected are absolutely blocked or not. If they are, one or both of them, the diagnosis of new growth should be made; the case should at once become a surgical one, and no further time be spent in "watchful waiting." A cholecystenterostomy at this time will be of greater assistance to the patient and prevent the dire consequences of a fully established malignant icterus. The mortality of this preliminary operation would probably be very much lower at this time than when performed months later.

Four to six weeks may safely be allowed to elapse. The nature of the growth permits of this delay, for it grows but slowly and has little tendency to metastases. With more assurance and a much better hope of success the second stage of the operation may be undertaken. The successful issue of the radical excision of new growths involving these large ducts will rest in great part on the alacrity with which the physician makes this early diagnosis and calls to his aid a competent surgeon.

GENERAL SUMMARY. In most of the new growths involving the bile and pancreatic ducts we are dealing with localized and relatively benign "rodent ulcers." The duodenal tube, in the great majority of cases, allows of early and absolute diagnosis. Delay, with its concomitant cholemia, hemorrhage, and rapid emaciation can thus be avoided and the powers of modern surgery be hopefully invoked to continue, with ever bettering results, a warfare on this type of malignant growth.

THE ABSORPTION OF PROTEIN AND FAT AFTER THE RESECTION OF ONE-HALF OF THE SMALL INTESTINE.

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STUDIES of absorption in cases with extensive resection of the small intestine have been made by several investigators. In August, 1913, Dr. E. A. Codman removed from a woman, aged forty years,

235 cm. intestine with tuberculous ulcers and strictures. Since the operation I have made certain observations which are of sufficient interest to report.

A housewife, now forty years old, with a family of five healthy children, presented the following history: In 1895 she was in the hospital with symptoms of hyperthyroidism, which quickly subsided. She had an acute appendix removed in 1910.

The patient entered the hospital June 20, 1913, on the east surgical service, complaining of cramp-like pains in the lower abdomen and a loss of eight and a half pounds in weight during the previous six weeks. There was some right-sided tenderness, which was considered voluntary. From the röntgen-ray plates Dr. Holmes made the diagnosis of probable extensive adhesions in the lower abdomen. Dr. Codman operated for chronic obstruction of the small intestine. At operation he found many tuberculous ulcers and strictures in the lower third of the small intestine and in the ascending colon. A jejunocolostomy was made. A good recovery from the operation followed, and while in the wards there was no gastro-intestinal disturbance. About a week after leaving the hospital's convalescent home, August 1, 1913, a distressing diarrhea, associated with lower abdominal cramps, began. There was no vomiting, and no blood had been noticed in the feces. Loss of weight and strength had been marked.

On August 30, 1913, the patient entered the east surgical service. About the umbilicus there was marked visible peristalsis. No masses could be felt. Dr. Codman performed a second operation, in which he resected the lower half of the small intestine and the ascending colon, making in all 235 cm. of resected intestine. It was thought that all the diseased intestine was removed. Also, it was estimated that at least half of the small intestine had been removed. The small intestine was joined to the colon by a lateral anastomosis. A good recovery from the immediate effects of the operation was made.

On September 25, 1913, the patient was transferred to the east medical service for regulation of diet. On a liquid and soft-solid diet there were daily two or three large, liquid, foul-smelling stools, showing an excess of fatty acids and soaps; little neutral fat and no mucus, pus, or blood was seen. At the suggestion of Dr. Edsall I carried out an absorption experiment at this time. (See Table I.)

At the time of leaving the hospital, October 15, 1913, after several days of low fat diet, she was gaining weight and passing daily one or two stools, which were fairly well formed. She was much better generally. Soon after leaving the hospital, however, she developed numbness and peculiar "drawing sensations" in the legs, forearms, and face. The family physician recognized the

condition as tetany, and sent the patient to the hospital October 27, 1913. Chvostek's, Trousseau's, and Erb's phenomena were all well marked. A second absorption experiment and in addition a study of the calcium metabolism were carried out. (See Table II.) Following the experiment she was given a diet low in fat and in addition 15 grains of calcium lactate four times a day. Toward the end of the metabolism experiment the tetany condition improved slightly. After the institution of the low fat diet and the use of calcium there was marked and rapid improvement, until on November 24, neither the Chvostek nor Trousseau phenomena could be elicited and the electrical reactions were normal. There was no numbness of the hands or face. She was passing one or two large semiformed stools a day. She left the hospital November 26.

During December following she had a good appetite and gained in weight and strength. In January and February, however, her appetite failed markedly, her stomach was "sour," and she began to lose weight. There had been no attacks of tetany. Suddenly, on February 24, she was seized with a severe attack of tetany, involving her legs, arms, and face. Three days later she entered the hospital, where again calcium was given, and in three days more the symptoms of tetany had disappeared. She went home after a two weeks' stay in the hospital. At this time the stools showed little change in the gross appearance, but microscopically there was more neutral fat than at her previous entries.

During March, April, and May, while at her home, she made little gain. Her appetite was capricious, she vomited frequently, and tetany symptoms were present in varying degrees most of the time. On May 20 the patient entered the hospital for the seventh time. Her general appearance was not as good as six months previously, but the weight, eighty pounds, was about the same. Trousseau's sign was easily elicited. There was no Chvostek's phenomenon. The electrical reactions were not secured. In the upper abdomen, directly above the umbilicus, lying transversely, was a sausage-shaped tumor about 7 cm. in length. A similar tumor could be made out under the scars of the previous operations. A third absorption experiment was carried out. Shortly after the end of the observations, without apparent cause, she became mildly delirious, with ideas of persecution, insisting on going home, which she was allowed to do.

The urine showed no albumin, sugar, acetone, or diacetic acid during the entire time she was under observation in the hospital. The Wassermann reaction on the blood was negative. Examination of the blood revealed nothing remarkable.

METHODS AND DIET. *Urine.* Total nitrogen, urea, and ammonia were determined according to Folin's new methods.¹ For uric acid

¹ Jour. Biol. Chem., 1912, xi, 493, 507, 523.

and creatinin the methods of Folin were used.² Creatin was determined by Folin's method.³ The colorimetric method described by Myers and Fine⁴ was used to estimate indican. For the hydrogen ion concentration the method of Henderson and Palmer,⁵ titratable acid, Henderson's method,⁶ and calcium, McCrudden's method,⁷ were employed.

Feces. In periods 1 and 2 large amounts of 95 per cent. alcohol were added to the fresh feces, which were dried on the water-bath to a constant weight. After pulverization nitrogen was determined by the usual Kjeldahl method; fat and fatty acid according to the method of Folin and Wentworth.⁸ In period 3 the nitrogen determinations were made on the fresh stools, which were kept frozen until the end of the experiment. The fat estimations were made after drying, as described above. To estimate the calcium in the feces the organic matter was destroyed by nitric and sulphuric acid after the method of Neumann⁹ and the determinations made as in the method of urine.

Diet. In periods 1 and 3 the diet consisted of eggs, bread, sugar, butter, and milk accurately weighed and the nitrogen and fat computed from the tables of Atwater and Bryant,¹⁰ with the exception that the fat and nitrogen in the milk were determined by analysis.

In period 2 the food was analyzed for nitrogen, fat, and calcium. The food mixture used was the one employed by Folin¹¹ in his work on normal urines:

Whole milk	500 c.c.
Cream (18 to 22 per cent. fat)	300 c.c.
Eggs (white and yolk)	450 gms.
Horlick's malted milk	200 gms.
Sugar	20 gms.
Sodium chloride	6 gms.

Water enough to make the whole up to two liters. In addition, soda crackers were allowed.

² Approximately Complete Analyses of Thirty "Normal" Urines, Amer. Jour. Physiol., 1905, xiii, 45.

³ Beitrag zur Chemie des Kreatinins und Kreatins im Harn, Zeit. f. Physiol. Chem., 1904, xli, 223.

⁴ Essentials of Pathological Chemistry, New York, 1913, p. 93.

⁵ The Intensity of Urinary Acidity in Normal and Pathological Conditions, Jour. Biol. Chem., 1913, xiii, 393.

⁶ A Critical Study of the Process of Acid Excretion, Jour. Biol. Chem., 1911, ix, 403.

⁷ The Determination of Calcium in the Presence of Magnesium and Phosphates; The Determination of Calcium in Urine, Jour. Biol. Chem., 1911, x, 197.

⁸ A New Method for the Determination of Fat and Fatty Acids in Feces, Jour. Biol. Chem., 1910, vii, 421.

⁹ Einfache Veraschungsmethode, Zeit. f. Physiol. Chem., 1903, xxvii, 117.

¹⁰ The Chemical Composition of American Food Materials, Bull. No. 28 (revised edition) United States Department of Agriculture, Office of Experiment Stations.

¹¹ Loc. cit.

TABLE I—Period 1.

Date, October	Volume of urine c.c.	Hydrogen ion concentration, ¹	Acid n/10 c.c.	Ammonia n/10 c.c.	Acid + ammonia.	Acid + ammonia.	Total nitrogen.	Urea - N.	Ammonia - N.	Creatinin - N.	Uric acid - N.	Nitrogen in feces.	Nitrogen in urine and feces.	In per cent. of total nitrogen.				Food.		Fatty acid in feces. ²	Weight in kilos.
														Urea.	Ammonia.	Creatinin.	Uric acid.	Nitrogen.	Fat.		
5-8	985	5.8	107	657	764	0.17	4.12	3.02	0.92	0.12	0.04			74	22	2.8	0.9				36.3
6-6	560	6.0	80	495	575	0.16	4.24	2.97	0.69	0.10	0.06			70	16	2.5	1.4				36.3
7-9	790	5.8	122	667	789	0.18	4.54	2.66	0.94	0.12	0.06	7.18	30.34	59	21	2.6	1.2	35.06	297.54	81.2	36.4
8-8	985	5.8	100	650	750	0.15	4.95	2.53	0.91	0.13	0.04			51	18	2.7	0.8				36.4
9	620	5.8	93	496	589.	0.19	5.31	3.73	0.70	0.12	0.04			70	13	2.2	0.7				36.5

¹ Expressed as the logarithm of the actual value, the minus sign being omitted.² Includes the soap. This holds in the remaining table.

TABLE II—Period 2.

Date, November	Volume of urine c.c.	Hydrogen ion concentration.	Acid n/10 c.c.	Ammonia n/10 c.c.	Acid + Ammonia.	Acid + Ammonia.	Total nitrogen.	Urea - N.	Ammonia - N.	Creatinin - N.	Uric acid - N.	Nitrogen in feces. ¹	Nitrogen in urine and feces.	In per cent. of total nitrogen.				Food.		Fatty acid in feces.	Calcium in food.	Calcium in urine.	Calcium in feces.	Weight in kilos.
														Urea.	Ammonia.	Creatinin.	Uric acid.	Nitrogen.	Fat.					
5-8	580	5.7	130	753	883	0.17	4.30	2.05	1.06	0.18	0.07			48	39	4.1	1.7							37.1
6-3	438	5.7	155	770	925	0.20	4.38	2.29	1.08	0.19	0.07			52	25	4.3	1.6							37.8
7-3	440	6.0	143	735	878	0.19	5.06	2.83	1.03	0.18	0.07	14.17	37.45	56	20	3.6	1.4	52.97	457.4	80.5	7.117	0.029	5.323	37.9
8-2	428	6.0	137	687	824	0.20	4.65	2.93	0.96	0.19	0.13			63	21	4.0	2.8							37.8
9	660	6.0	135	635	770	0.21	4.89	3.12	0.88	0.20	0.12			64	18	4.0	2.4							38.0

¹ Owing to the large amounts of free ammonia in the stools (as much as 0.43 gm. ammonia-nitrogen in a single stool) there was undoubtedly considerable stool nitrogen lost in the method of preparation for analysis.

TABLE III.

Date.	Volume of urine c.c.	Specific gravity.	Hydrogen ion concentration.	Acid n/10 c.c.	Ammonia n/10 c.c.	Acid + ammonia n/10 c.c.	Acid ÷ ammonia.	Ammonia — N.
9 November	540	1016	5.8	75	488	563	0.15	0.68
10	845	1010	5.8	127	508	635	0.25	0.71
11	805	1013	5.9	148	494	642	0.30	0.69
12	359	1022	5.6	104	376	480	0.28	0.53
13	545	1012	5.7	104	328	432	0.32	0.46
14	935	1007	5.3	59	304	363	0.20	0.43
15	450	1017	5.5	113	346	459	0.33	0.49
16	1050	1007	5.7	65	346	411	0.19	0.49
17	855	1010	5.9	68	264	332	0.26	0.37
18	875	1010	5.8	111	265	379	0.43	0.37

TABLE IV—Period 3.

Date.	May	Volume of urine c.c.	Hydrogen ion concentration.	Acid n/10 c.c.	Ammonia n/10c.c.	Acid + am- monia.	Acid + am- monia.	Total nitrogen.	Urea - N.	Ammonia - N.	Creatinin - N.	Creatinin - N.	Creatin - N.	Creatin + Crea- tinin - N.	Uric Acid - N.	Indican.	In per cent of total nitrogen.						Food.				Nitrogen in urine and feces.	Weight in kilos.
																	Urea.	Ammonia.	Creatinin.	Creatin.	Creatin - creatinin	Uric acid.	Nitrogen.	Fat.	Nitrogen in feces.	Fat in feces.		
25		420	6.1	156	650	806	0.24	5.33	3.26	0.91	0.23	0.053	0.029	0.06	0.07	0.80	63	17	1.3	1.0	5.4	1.2	36.6	
26		460	6.0	200	785	988	0.26	5.30	3.26	1.10	0.23	0.100	0.33	0.75	0.75	0.80	51	22	4.6	2.0	6.6	1.1	36.3	
27		300	6.0	215	915	1130	0.24	6.05	3.33	1.28	0.23	0.096	0.33	0.06	0.06	0.50	58	21	3.8	1.6	5.4	1.0	35.7	
28		265	5.7	190	650	840	0.29	4.39	3.33	0.91	0.20	0.048	0.25	0.02	0.02	0.69	56	20	4.4	1.0	5.5	0.3	35.6	
29		185	6.0	214	880	1094	0.24	4.69	4.55	1.33	0.22	0.048	0.17	0.05	0.05	0.72	67	18	3.2	0.7	3.9	0.7	35.5	

TABLE V—Summary of Results.

Period.	Food nitrogen.	Urine nitrogen.	Feces nitrogen.	Per cent. nitrogen ingested lost in feces.	Nitrogen balance.	Food fat.	Total feces fat.	Fatty acid in feces. ¹	Per cent. fat ingested lost in feces.	Per cent. fatty acid lost in feces. ¹
1	35.06	23.16	7.18	20.4	+1.71	297.54	82.2	60.5	27.3	73.6
2	52.97	23.28	14.17	21.1	+15.52	129.0	129.0	80.5	28.2	62.4
3	50.80	27.91	12.67	25.0	+10.22	443.7	136.0	51.7	30.7	38.0

¹ Includes the soaps.

DISCUSSION. Extensive resections of the small intestine with recovery have been reported from time to time. In 1912 Flint¹² gathered together the cases, 59 in all, in which 200 cm. or over had been resected, giving reference and result in each case. Repetition of these cases is unnecessary. The most remarkably extensive resection yet reported is by Denk,¹³ in a woman, aged sixty-one years, from which 540 cm. (21 feet 3 inches) of the small intestine were removed. A good recovery without intestinal disturbance is claimed for this patient. This extraordinary case stands alone in the literature, and one should be cautious in accepting it as a criterion for maximum resection.

The effect on absorption and metabolism of extensive resection of the small intestine has been studied experimentally in animals by Senn,¹⁴ Monari,¹⁵ Trzebicky,¹⁶ Erlanger and Hewlett,¹⁷ and Flint.¹⁸ There is a general agreement among these investigators that half of the small intestine in dogs may be removed without seriously affecting growth of metabolism. As much as 75 per cent. of the intestine has been removed, with recovery, but the dogs usually die from inanition, due to uncontrollable diarrhea. Monari, however, makes the statement that seven-eighths of the small intestine may be resected without serious impairment.

Metabolism studies following extensive resection of the intestine in men have been made in a few cases, which were reviewed in 1910 by Mijaki¹⁹ and again in 1912 by Flint.²⁰ The grade of metabolic disturbance, both in men and in animals, appears not to be wholly dependent on the length of intestine resected, but in part on certain indeterminable factors. The results of animal experimentation are suggestive and important, but care is necessary in the interpretation of their significance in human physiology. It must be remembered that not all cases of intestinal resection in men are comparable to animal resections. Very frequently there are diseased conditions of the intestine in men not reproduced or that are not reproducible in animals. In men the condition of the intestine is of the utmost importance and should be carefully considered whenever extensive resections are contemplated. The greater the certainty of leaving nothing but healthy intestine the more frequently may extensive

¹² The Effect of Extensive Resection of the Small Intestine, *John Hopkins Bull.*, 1912, xxiii, 127.

¹³ Ausgedehnte Darmresektion mit Ausgang in Heilung, *Wiener klin. Woch.*, 1907, xx, 1649.

¹⁴ *Experimental Contributions to Abdominal Surgery*, Chicago, 1892.

¹⁵ Experimentelle Untersuchungen über die Abtragung des Magens und Dünndarms beim Hunde, *Beiträge z. klin. Chir.*, 1896, xvi, 479.

¹⁶ Ueber die Grenzen der Zulässigkeit der Dünndarmresektion, *Arch. f. klin. Chir.*, 1894, xlviii, 54.

¹⁷ A Study of the Metabolism in Dogs with Shortened Small Intestines, *Amer. Jour. Physiol.*, 1901, vi, 1.

¹⁸ *Loc. cit.*

¹⁹ Ueber ausgedehnte Darmresektion, *Arch. f. klin. Chir.*, 1910, xciii, 768.

²⁰ *Loc. cit.*

resection be successfully undertaken. It would seem doubtful, if even under the most favorable circumstances, more than half of the small intestine should be removed in human individuals. I am well aware that in certain acute conditions, such as volvulus, intussusception, and incarcerated herniæ, where there is beginning gangrene the surgeon is left no choice and must take the chance.

In men and animals alike fat absorption is most disturbed, nitrogen less interfered with, and carbohydrates are nearly always absorbed in a normal manner. The highest percentage, 34.2, of nitrogen loss in the feces is found in Axhausen's case,²¹ in which 475 cm. of small intestine were resected. The nitrogen found normally in the feces, according to Schmidt and Strasburger,²² is 4 to 6 per cent. Zuseh²³ reports the highest percentage, 38, of fat lost in the feces. Schmidt and Strasburger give the average daily loss of fat in the stools of a normal individual taking a mixed diet as 4 to 6 per cent. of the intake. According to these observers, and also Folin and Wentworth,²⁴ 60 to 70 per cent. of the fat recovered in the stools is in the form of fatty acid. The loss of both fat and nitrogen in our case is marked. The nitrogen loss, 20.4 per cent., in period 1, 21.1 per cent. in period 2, 25 per cent. in period 3, is four to five times the normal loss. Even a greater loss in fat occurs, 27.3 per cent. in period 1, 28.2 per cent. in period 2, 30.7 per cent. in period 3, which is five or six times the loss in normal individuals. There occurs a marked reduction in the percentage of fatty acids in the stools, 73.6 per cent. in period 1, 62.4 per cent. in period 2, and 38 per cent. in period 3. The progressively poorer absorption of fat and nitrogen, together with the reduction in the degree of saponification in the stool, is probably due to the progress of the tuberculous condition in the intestines.

In the distribution of the urinary nitrogen among urea, ammonia, uric acid, and creatinin the high percentage of ammonia with a relatively low urea is at once noticeable. Folin²⁵ in his analyses of thirty normal urines found 3.3 to 5.1 per cent. ammonia-nitrogen with the urinary total nitrogen ranging between 14.8 to 18.2 gms., 4.2 to 11.7 per cent. where the urinary nitrogen varied between 4.8 to 8 gms. In my case in period 1, the urinary nitrogen varying between 4.1 and 5.2 gms., the ammonia-nitrogen was between 13 and 22 per cent. In period 2 a greater range of 18 to 39 per cent. ammonia-nitrogen, with 4.3 to 5 gms. of urinary nitrogen, occurs. The urinary nitrogen is slightly higher in period 3, 4.5 to 6.9 gms., and the ammonia-nitrogen varies between 18 and 22 per cent. Uric acid and creatinin in periods 1 and 2 do not vary markedly

²¹ Axhausen, G. Ueber die obere Grenze f. die Zulässigkeit ausgedehnter Dünndarmresektion, Mitteil. u.d. Grenzgeb. der Med. u. Chir., 1909 10, xxi, 55.

²² Die Fäzes des Menschen, Berlin, 1901.

²³ Stoffwechsel nach ausgedehnter Dünndarmresektion, Berl. med. Woch., 1901, xxxv, 739.

²⁴ Loc. cit.

²⁵ Loc. cit.

from the normal, both being quite constant from day to day. There is, however, a gradual increase in the absolute amount of creatinin during the three periods, as may be seen on examination of the tables. In period 1 the daily average creatinin-nitrogen excretion is 0.118 gm., period 2, 0.188 gm., and in period 3, 0.222 gm. During the investigation there was no marked change in weight. There is not sufficient data available to determine the significance of this. The increased metabolism known to occur in tuberculosis is undoubtedly an important factor. In period 3 creatin appears in the urine for the first time. The creatinin, however, is very constant. The appearance of creatin is probably explained by the fact that the patient had a temperature varying between 99° and 100° during the experiment. The progress of the tuberculous condition in the intestine may also have been a factor. On the fourth day of the experiment, May 29, both creatinin and uric acid are low. Careful inquiry failed to reveal any loss of urine, but this possibility is not absolutely ruled out.

Especially interesting is the indican excretion. The excretion of indican in normal individuals in twenty-four hours is usually given as 10 to 50 milligrams.²⁶ Hawk and his collaborators²⁷ have found as much as 114 mg. in twenty-four hours. On the first day of period 3 my patient excreted 800 mg. of indican, an amount in excess of any thus far reported.²⁸ Indican has been considered for a long time an index of the degree of intestinal putrefaction.

A study of the acid factors of the urine has brought to light little that is not revealed in the nitrogen constituents. The hydrogen ion concentration varies very little, and is within the normal limits as reported by Henderson and Palmer.²⁹ The ammonia is high when compared to the acid. This, of course, makes the acid-ammonia ratio varying between 0.15 and 0.29 much lower than the normal of 0.75 reported by Henderson and Palmer.³⁰ The low ratio is evidently due to the increase in ammonia rather than any decrease in acid excretion. Following period 2 the acid factors were studied for several days. (See Table III.) A steady and marked reduction in the ammonia occurs. During this time the tetany was improving rapidly. Increase in the ammonia excretion has been found to occur in tetany by MacCallum and Voegtlin³¹ and

²⁶ Neubauer-Huppert's *Lehrbuch. Analyse des Harns*, Elfte Auflage, Wiesbaden, 1913, xi, 797.

²⁷ Intestinal Putrefaction during Copious and Moderate Water-drinking with Meals, *Arch. Int. Med.*, 1911, vii, 610, Sherwin, C. P., and Hawk, P. B.: The Putrefactive Processes in the Intestine of a Man during Fasting and during Subsequent Periods of Low and High Protein Ingestion, *Jour. Biol. Chem.*, 1912, xi, 169.

²⁸ Dr. Denis informs me that she has found as much as 500 mg. of indican in a twenty-four-hour specimen of urine.

²⁹ *Loc. cit.*

³⁰ The Several Factors of Acid Excretion, *Jour. Biol. Chem.* 1914, xvii, 305.

³¹ The Relation of Tetany to the Parathyroid Glands and to Calcium Metabolism, *Jour. Exp. Med.*, 1909, xi, 118.

others. Some form of acidosis was suggested by the high ammonia. Accordingly following period 3, sodium bicarbonate as a test for acidosis, suggested by Palmer and Henderson³² were employed. There was no reduction in urinary acidity after 5 grams of sodium bicarbonate by mouth, nor was there any change in the titratable acid or ammonia. After the ingestion of 10 grams of sodium bicarbonate, while the hydrogen ion concentration showed no change, there was some reduction in both titratable acid and ammonia. It was not possible to study the effect of larger doses because of the unwillingness on the part of the patient to continue the experiment. Acetone bodies were persistently absent from the urine in all the periods. It seems justifiable to conclude that there was no marked acid intoxication to explain the high urinary ammonia.

In connection with the increased urinary ammonia the ammonia in the stools is interesting. During period 2 as much as 0.43 gm. in a single stool was found. That the extensive putrefaction in the intestine may be largely responsible for the high ammonia in the urine seems not improbable. Folin and Denis³³ found in their cat experiments that the large part of the ammonia which was converted into urea in the liver came from the large intestine, and apparently was the result of putrefaction. It is quite possible that more ammonia escapes conversion into urea than normally, due to the large amount or to incompetency on the part of the liver.

The observations on the calcium metabolism in the second period were made because of the tetany. Normally, calcium is excreted largely by the bowel. During tetany following parathyroidectomy there is a marked loss of calcium from the body. The importance of calcium in these experimental conditions is further illustrated by the remarkable improvement following its administration.³⁴ The various studies of calcium metabolism, however, with all the difficulties encountered, leave one in doubt as to its exact significance in the several conditions in which tetany is met. It is interesting in my case that during the five days, a total of only 29 mgs. was excreted in the urine. This low amount of calcium in the urine may be explained in part by the rapidity with which the food passed through the intestinal tract, or the diseased condition of the intestine may be a factor. The absorption of small amounts of calcium and possibly the presence of an insufficient amount in the body, as a factor in the causation of the tetany, is suggested by these observations, but by no means proved. It should be remembered that there occurred definite improvement in the tetany in period 2 before calcium was given.

³² Clinical Studies in Acid Base Equilibrium and the Nature of Acidosis, *Arch. Int. Med.*, 1913, xii, 153.

³³ The Origin and Significance of the Ammonia in the Portal Blood, *Jour. Biol. Chem.*, 1912, xi, 161.

³⁴ MacCallum, W. G., and Vøgtlin, Carl, *loc. cit.*

SUMMARY. 1. Absorption studies after resection of the lower half of the small intestine are reported.

2. The loss of nitrogen in the stools is four to five times that of normal individuals.

3. The loss in fat in the stools is five to six times the normal loss.

4. A high urinary indican, 800 mgs. is reported.

5. Ammonia forms a much larger part of the urinary nitrogen than in normal individuals. This is probably due to the extensive putrefaction taking place in the intestine.

6. The success with which a large portion of the intestine may be removed depends to a large degree on the condition of the intestine remaining. This fact I believe to be important and should be considered carefully before extensive resections are undertaken.

7. A diet low in fat and moderately low in protein should be given in cases where much intestine has been removed.

I wish to thank Dr. Edsall for his kindly interest and many valuable suggestions during the investigation.

THE RÖNTGENOLOGIC METHOD OF DIFFERENTIATING BETWEEN ULCER AND CANCER OF THE STOMACH AND DUODENUM.

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DURING the past two years I have heard several eminent gastroenterologists and internists, as well as numerous general practitioners, make statements in the public discussion of scientific papers concerning the röntgenologic diagnosis of ulcers of the stomach and duodenum which showed that there is a widespread belief that these lesions are evidenced by a single irregular bismuth shadow. The commonest errors noted were diagnoses based on a "persistent bismuth fleck," a "spasmodic or organic hour-glass of the stomach," or a "gastric bismuth residue after six hours."

PRELIMINARY REMARKS. We recognize that anatomically and physiologically the first portion of the duodenum is not considered a part of the stomach, but symptomatically and surgically it is perhaps the most important part. It is rarely visible fluoroscopically, and in order to obtain its röntgenographic picture, buttermilk instead of gruels must be used for suspending the opaque meal. Since the first portion of the duodenum is embryologically, symptomatically, surgically, and röntgenographically a part of the

stomach, the word gastric, as used in this communication, will refer to the first portion of the duodenum as well as to the stomach itself.

RÖNTGENOGRAPHIC APPEARANCE OF GASTRIC (AND DUODENAL) ULCERS. The main object of this paper is to describe the roentgenographic appearance of ulcerative lesions of the stomach and to point out the differential diagnostic points between malignant and non-malignant processes. Hemmeter¹ was the first to describe the findings of gastric ulcer. He claims that an isolated fleck in the gastric region, visible in roentgenograms made several hours after all the rest of the opaque meal has left the stomach, is evidence of a bismuth deposit adherent to an ulcerated surface. Kreuzfuchs² and Ashbury³ also attribute this phenomenon to gastric ulcer, or to duodenal ulcer if observed in the duodenal region. This theory has gained wide acceptance, and it may be true in certain cases. There are many more cases of ulcer in which the sign does not present.

According to Holz knecht⁴ simple gastric ulcer is characterized by (1) small residue after six hours, (2) sensitive pressure point over the stomach, (3) normal gastric shadow. The diagnosis may be confirmed further by (4) presence of active peristalsis (hyperperistalsis), (5) displacement of the pylorus upward and to the left, (6) snail form of the lesser curvature, (7) stabile transverse contraction. Holz knecht's conclusions are evidently drawn from fluoroscopic observations or from a small number of roentgenograms in each case and not from roentgen plates taken serially, as he depends on secondary manifestations rather than on direct visualization of the lesion defect.

Haudek⁵ describes a direct visualization of a lesion defect in his diverticulum bismuth shadow and gas outline (nischen symptom) which in his opinion indicates a callous penetrating ulcer. In diagnosing non-penetrating ulcers of the stomach he recognizes those: (1) Showing diverticulum outside of the bismuth shadow; (2) not showing such a diverticulum, but a slight drawing in of the greater curvature opposite the ulcer, and a point of localized tenderness over the lesser curvature, which moves with respiration.

Strauss⁶ has recently published an article on duodenal ulcer, in which he cites a symptom complex with nine subdivisions, which do not altogether agree with Holz knecht's observations.

¹ Priority of Employment of the Röntgen Ray in Studying the Physiology and Pathology of the Digestive Tract, Jour. Amer. Med. Assoc., October 5, 1912; Neue Methoden zur Diagnose des Magengeschwüers, Arch. f. ver. b., xii H 5.

² Concerning the Technique of the Röntgen Investigation of Duodenal Ulcer, Berl. klin. Woch., 1912, Nr. 33.

³ Röntgen Ray Findings in Gastric and Duodenal Ulcer, Amer. Quart. of Rönt., December, 1911. The Röntgen Ray Diagnosis of Ulcer of the Stomach and Duodenum, Adler and Ashbury, New York Med. Jour., October 7, 1911.

⁴ The Röntgen Diagnosis of the Stomach, Arch. of Rönt. Ray, November, 1911.

⁵ The Röntgen Diagnosis of Chronic Gastric Ulcer, Arch. of Rönt. Ray, June 1911.

⁶ Das Duodenal ulkus und seine Feststellbarkeit durch Roentgenstrahlen, Fort. a. d. Geb. d. Roentgenstrahlen, 1913, B. xix, H. 6, S. 151.

Cole⁷ reports that by his method of serial roentgenography he gets direct visualization of the lesion defect and is able to detect the slight deformities caused by small lesions which can be recognized only by making a large number of roentgenograms. According to Cole the presence of gastric ulcer is manifested by (1) constant defects of bismuth outline, (2) obliteration of normal pyloric or duodenal outlines, (3) a constant interference with the peristalsis as it progresses pylorusward. He regards the presence of abnormally prominent rugæ near the lesion as indicative of adhesions and therefore as confirmatory evidence of ulcer.

Carman⁸ in a recent article from the Mayo clinic emphasizes the importance of hyperperistalsis as a diagnostic sign in duodenal ulcer.

It is only fair to assume at the present time that no single irregularity of the bismuth shadow or persistence of bismuth is characteristic of an ulcer, but that the diagnosis of ulcer of the stomach or duodenum is a complex matter of interpretation, as the lesion may present various roentgenologic manifestations.

DIFFERENTIAL DIAGNOSIS OF GASTRIC (AND DUODENAL) ULCER AND GASTRIC CANCER. The differential diagnosis of gastric (and duodenal) ulcer and gastric cancer depends largely upon the following classification:

RÖNTGEN CHARACTERISTICS.

GASTRIC ULCER (including duodenal) ⁹	Acute (Fig. 1).	{ Small stabile defect in bismuth shadow. Associated with spasm.
	Chronic (Fig. 2).	{ Larger stabile defect in bismuth shadow. Associated with cicatricial formation. Associated with stenosis. Associated with dilatation.
GASTRIC CANCER (including duodenal) ¹⁰	Transitional	(Fig. 3) from ulcer to cancer. Can only be differentiated from ulcer by microscopic examination.
	Papillary (Fig. 4).	{ Small defect in bismuth shadow similar to ulcer.
	Medullary (Fig. 5).	{ Commonest form of cancer, lesion large and easily diagnosed by rentgen examination.
	Scirrhus (Fig. 6).	{ Fixed, contracted stomach, lesion easily diag- nosed.

⁷ Serial Radiography of the Stomach and Duodenum, Arch. of Rent. Ray, December, 1911, April, 1912, October, 1912; The Diagnosis of Postpyloric (Duodenal) Ulcer by Means of Serial Radiography, read at Int. Cong., London, August, 1913.

⁸ Radiologic Signs of Duodenal Ulcer, Jour. Amer. Med. Assoc., March 28, 1914, vol. lxii, No. 13, p. 980.

⁹ Duodenal ulcer is much more common and characteristic in its rentgen outlines than gastric cancer.

¹⁰ Duodenal cancer is very rare. I have never observed a case. If seen early enough it would probably have the same rentgen characteristics as acute ulcer, and later the same rentgen characteristics as gastric cancer.

	ULCER.	CANCER.	
<i>Visualization.</i>	Small and recent, may be overlooked on screen.	Much more easily recognized on screen.	
<i>Pain.</i>	Sharply localized pain-point, which moves synchronously with respiration and has direct and constant relation to defect in bismuth shadow. Presents early.	Pain diffuse, if any, and apt to present late.	
<i>Esophagus.</i>	No retention in esophagus, showing that walls of cardia are pliable.	Frequent retention in esophagus, showing that walls of cardia are stiffened and not pliable.	
<i>Multiple contours.</i>	Not present in ulcer.	Scalloped contours Finger-print contours Conical contours Superimposing test	} Significant.
<i>Hour-glass.</i>	Sacculated form of hour-glass. { Sulcus band-like. Segments equal. Spasm. Cicatrix.	Funnel-like form of hour-glass. (Fig. 5.)	
<i>Pyloric stenosis.</i>	Often causes pyloric stenosis, accompanied by hyperperistalsis and later dilatation.	May or may not cause stenosis and residuc, according to location and character. If at pylorus, neoplasm is apt to break down, become tunneled and infiltrate in the walls, so as to open the pylorus. Carcinoma of the lesser curvature frequently presents so advanced as to be inoperable without affecting the pyloric outlet.	
<i>Residuc.</i>	Ulcer often causes pylorospasm and six-hour retention because of hyperacidity.	Cancer seldom causes pylorospasm and retention because of anacidity.	
<i>Parasecretion.</i>	Zone of parasecretion between magenblase and bismuth shadow, showing hyperacidity.	Zone of parasecretion not shown because of anacidity.	
<i>Size of bismuth shadow of stomach.</i>	Acute ulcer: Bismuth shadow diminished — (minus), due to spasm and defect in contour. Chronic ulcer with stenosis and dilatation: Bismuth shadow increased + (plus)	Bismuth shadow usually diminished — (minus) or shows a marked filling defect.	
<i>Peristalsis.</i>	Hyperperistalsis if pylorus is involved.	Diminished or absent peristalsis on account of fixation.	
<i>Retroperistalsis.</i>	Retroperistalsis may present.	Seldom seen.	
<i>Height of stomach.</i>	Stomach usually not so high.	Stomach usually high in epigastrium.	
<i>Persistent bismuth speck.</i>	Hemmeter's persistent bismuth shadow characteristic when seen. Presents only rarely.	Hemmeter's persistent bismuth shadow may present.	
<i>"Nischen symptom."</i>	Haudek's "nischen symptom" characteristic of a pocket when seen. Presents rarely.	Haudek's "nischen symptoms" may be present, though rarely.	

Hemmeter's adherent bismuth shadow is pathognomonic of a small pocket, but not necessarily of ulcer. They present in both gastric ulcer and cancer and are determined by the topography of the lesion rather than by its morphology.

The differential diagnosis between an indurated ulcer and one which is undergoing carcinomatous degeneration can be made only by a microscopic examination of a section, so that for all practical purposes the indications for surgical procedure are the same for both types of involvement.

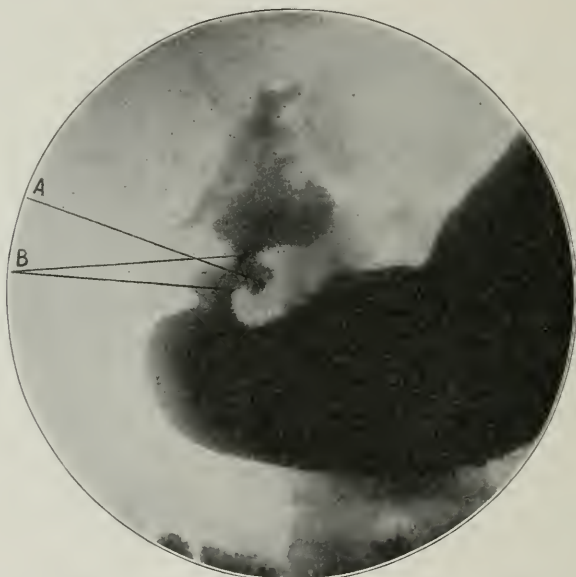


FIG. 1.—Acute gastric ulcer, characterized by a small, stable defect in the bismuth shadow, associated with spasm. Such a perfect profile or cross-section view as shown in this case is unusual. This bismuth defect was constant in more than 40 plates. The crater of the ulcer is usually not visible but the position of the ulcer is, as a rule, indicated by a constant absence of the peristaltic wave in the area of induration. A, crater of ulcer; B, walls of ulcer. (Case of Dr. L. G. Cole.)

We have dwelt at some length on the diagnosis of ulcers of the stomach and duodenum because: (1) Clinically the diagnosis of these cases is often obscure, and the question of operative or non-operative procedure must be determined according to the diagnosis by the physician in charge. (2) As a rule, ulcers are among the smallest lesions occurring in the stomach and duodenum, and, therefore, the diagnosis of this condition is the most difficult from a roentgenologic standpoint. (3) Many members of the medical profession appear to have formed an incomplete idea of the roentgenographic appearance of an ulcer from the reported phenomenon of bismuth, adherent to the lesion, or a bismuth residue after six hours.

WHY THE RÖENTGEN METHOD HAS BEEN CRITICISED. The fact that the lumen and motor phenomena of the gastro-intestinal tract can be visualized by the röntgen rays is now well established; the correct interpretation of variations from the normal shadows, however, is a fertile field for scientific investigation, and needs careful study, free from imagination. Only such facts as have been checked up by operation should be published. Criticism of the

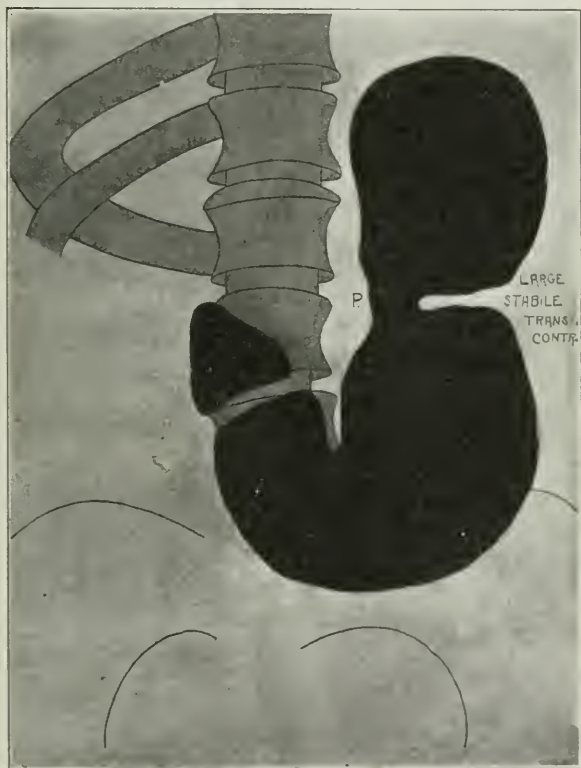


FIG. 2.—Drawing from a fluoroscopic tracing in a case of chronic gastric ulcer, in pars media, illustrating the coincidence of the "painful pressure point" (*P*), with a point on the lesser curvature of the stomach (site of the ulcer); opposite a large, stabile, transverse contraction, associated with cicatricial stenosis, atony, hypoperistalsis, pyloroptosis. No "residue after six hours," no "persistent localized bismuth fleck hours after ingestion." Duodenum normal.

röntgenologic method of diagnosis comes almost invariably from those who have had experience with incomplete, faulty, and too economical modifications of röntgen technique, or from erroneous interpretation of findings by inexperienced or overambitious persons.

EXPENSE. The only valid objection which can be raised to röntgen-ray examination is the great expense it entails. The limitation of the patient's purse is the only contra-indication. The

high cost of roentgenologic examination is due to (1) expensive and ever-improving models of roentgen-ray apparatus; (2) variation in

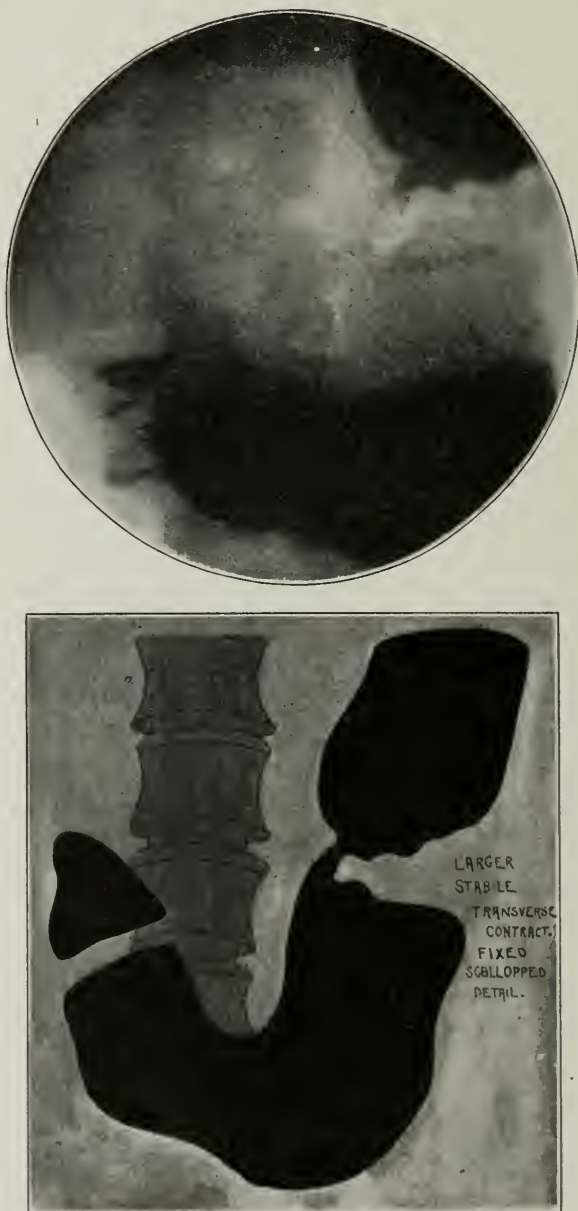


FIG. 3.—Chronic gastric ulcer in pars media. Characterized by a large stable transverse contracture and fixed scalloped detail suggestive of a transitional condition. Lower picture is a fluoroscopic tracing of the same case.



FIG. 4.—Papillary carcinoma of stomach, small, constant defect in the bismuth shadow, similar to ulcer, can only be differentiated by microscopic examination.

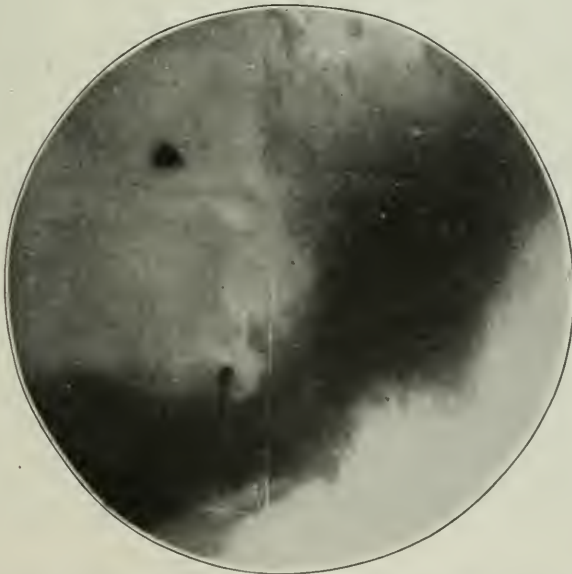


FIG. 5.—Medullary carcinoma of the stomach, characterized by a large, constant defect in the bismuth shadow. In successive plates these defects accurately fit over each other, as can be shown by superimposing one plate upon another and having the defects exactly fit over each other. This is called the "superimposing test." This case also illustrates the "funnel-shaped" hour-glass stomach characteristic of malignancy. (Case of Dr. L. G. Cole.)

individual requirements, so that skilled hand labor at high prices is demanded; (3) large quantities of expensive photographic materials necessary.

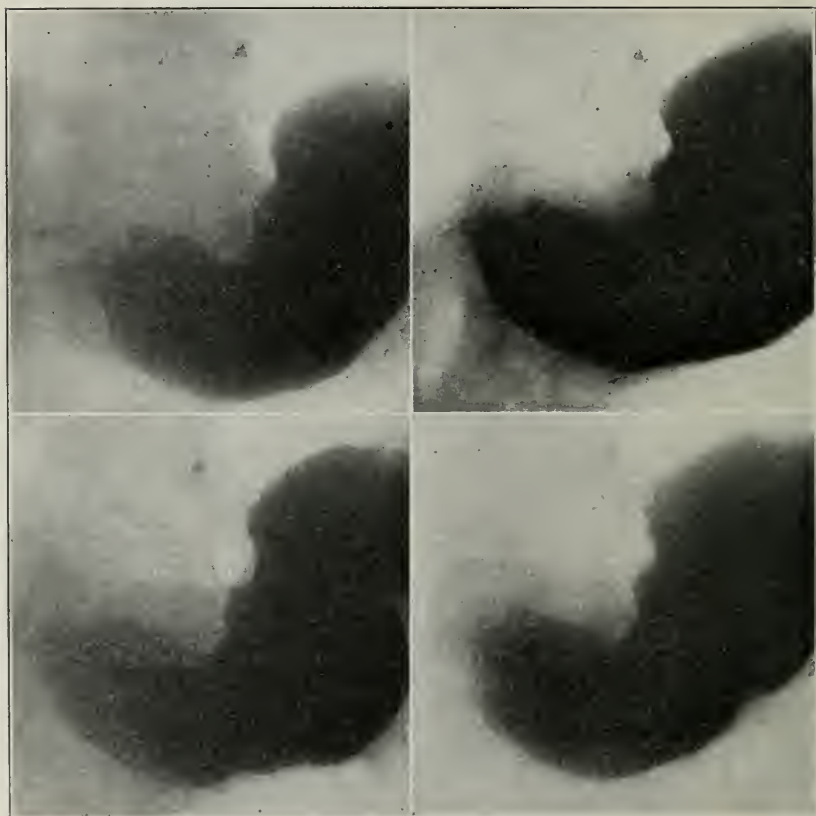


FIG. 6.—Scirrhus carcinoma of the stomach, characterized by a fixed, contracted stomach of small size. In this instance the lesion is located on the lesser curvature, and its edges look very much like peristaltic waves; however, when the superimposing test is applied it is found that these "waves" are not waves, because they do not move but always present as fixed bismuth defects. Note that there are no symmetrical peristaltic contractions on the greater curvature corresponding to these pseudo-waves. The diagnosis in these cases of scirrhus of the stomach and transitional carcinoma of the stomach when the lesion is located on the lesser curvature is impossible to make without a series of plates and the application of the superimposing test, because of the similarity between the bismuth defects caused by them and normal peristaltic waves.

The costliness of electrical apparatus, photographic materials, and skilled hand labor is a matter of common knowledge; thus more capital is required for the practice of roentgenology than for any other specialty. In one hospital where accurate records are kept the cost of making a single roentgenogram was the same as the cost

of doing an hysterectomy, and in examinations requiring more than two plates the outlay to the institution exceeded the cost of the

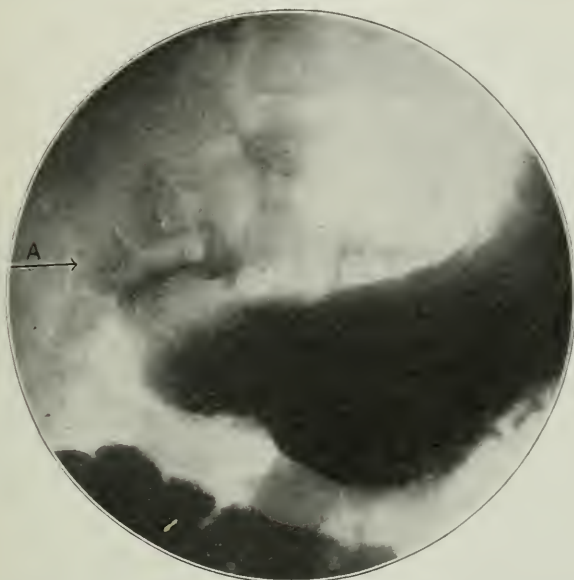


FIG. 7.—Clinically a case of gastric ulcer. Röntgenogram shows the typical outline of a spasmodic contraction of the first portion of the duodenum. Negative diagnosis of either gastric or duodenal ulcer made from the röntgen examination. Patient developed an acute appendicitis shortly afterward; a gangrenous appendix was removed, after which all gastric symptoms disappeared. A, spasm of duodenum.

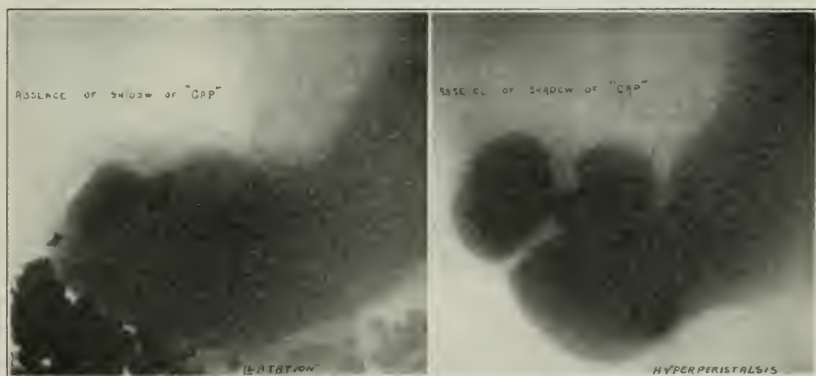


FIG. 8.—Typical appearance of chronic duodenal ulcer, characterized by absence of the shadow of bismuth in the first portion of the duodenum, hyperperistalsis, dilatation. Note the absence of the shadow of the first portion of the duodenal "cap."

average major operation. Institutions such as colleges and hospitals have not been educated to bearing this burden, as they have

learned to support the expense of the operating-room. In this country the cost of the experiments which have been made in developing röntgen diagnosis to its present prominence has been borne mainly by individual physicians and by manufacturers of röntgen-ray apparatus without the assistance of institutions. There appears to be no relief from this situation unless the röntgen-ray should prove to be of some commercial utility, and, having passed the experimental stage, become standardized.

FIG. 9



FIG. 10



FIG. 9.—Case of penetrating callous gastric ulcer illustrating the "nischen symptom" of Haudek, also stabile transverse contraction of an hour-glass stomach.

FIG. 10.—Same case after a gastrogastrostomy was performed and illustrating the necessity of having postoperative röntgen examinations made of our abdominal cases if we are to check up the effectiveness of our operations. In this class of cases a gastropasty would seem to offer better results than gastrogastrostomy.

The extra expense of serial röntgenography may be avoided if the diagnosis is perfectly evident from the fluoroscopic examination, and confirmatory diagnostic outlines are obtained on a few plates. There is danger, however, in thus adopting the more economical procedure as the routine method of examination, since many cases, presenting only slight lesions, will inevitably slip by as normal; and it is the diagnosis of these very cases which is most worth while, they being the ones most amenable to treatment. If, however, they pass unrecognized for the time being the surgical prognosis grows steadily worse, and when at last the diagnosis becomes unmistakable, these cases are the ones certain to be cited as instances in which the röntgen examination failed. Another pitfall is the danger of

mistaking spasmodic conditions for actual primary lesions. Such diagnostic errors are most apt to be made in cases of acute duodenal

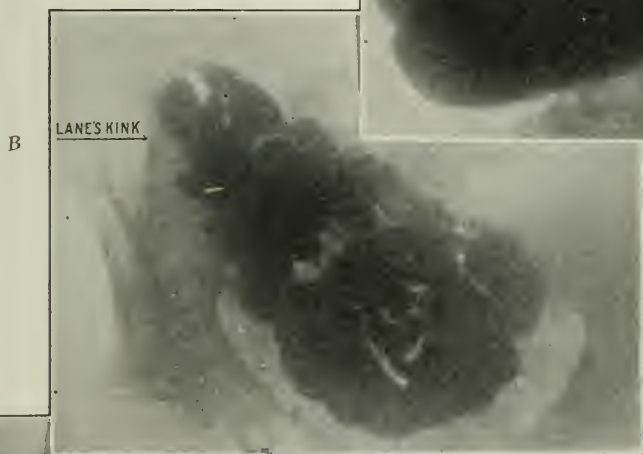
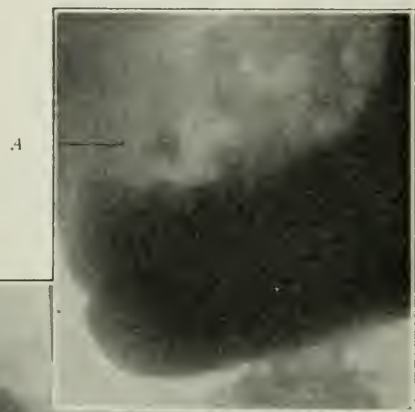


FIG. 11.—Defect in the bismuth shadow of the first portion of the duodenum, simulating the roentgen appearance of duodenal ulcer (*A*). In reality there was a case of Lane's kink (*B*), which caused a spasmodic contraction of the first portion of the duodenum. The normal appearance of the "cap" after the patient's bowels were cleaned out and a dose of tincture of belladonna administered is seen in (*C*).

or gastric ulcers, papillary carcinoma, and reflex spasmodic conditions secondary to lesions distant from the seeming lesion defect.

In extensive carcinoma of the lesser curvature, the outlines are often so regular that they are mistaken for peristaltic waves.

The roentgenologic method of examining the stomach and duodenum is much simpler, safer, more natural, and pleasanter to the patient than the use of the stomach tube or duodenal bucket, and the results obtained have been found more constant and reliable than the analysis of gastric or duodenal contents. When possible

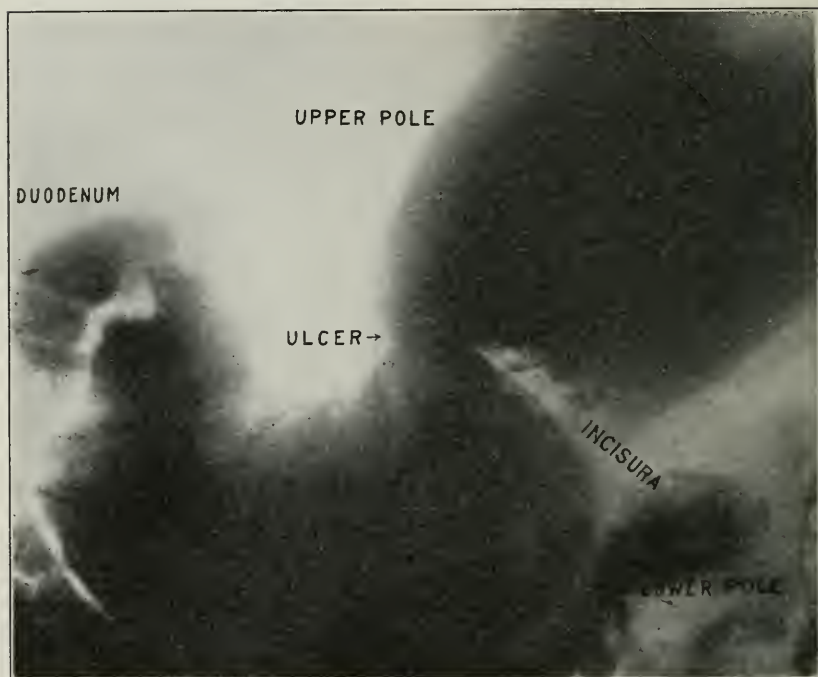


FIG. 12.—Gastric ulcer, chronic, with marked hour-glass contraction and atony. Patient had also extreme scoliosis. Pending decision as to operation, patient was reported to have developed a marked tumor in the right iliac fossa for which it was determined to operate. At operation the tumor was found to be an enormous accumulation of bismuth in an atonic cecum. This patient had had thorough catharsis and enemata administered, and sufficient time had elapsed since the initial roentgen-ray examination, so that a bismuth stasis was not suspected. This case also illustrates the value of pre-operative roentgen examinations, as such an examination of the cecum would have saved this patient from an operation.

in cases of suspected ulcer or where there is danger of perforation or hemorrhage the patient should not be submitted to the dangers attendant upon gastric or duodenal analysis until roentgenologic methods have been used first and have failed to give the desired information.

SURGICAL INDICATIONS. The ultimate decision as to operability rests with the surgeon, but the roentgen method will render him much assistance in drawing his conclusions for or against operation,

and in predetermining the best method of procedure. In cases of gastric ulcer, for instance, he gains such valuable information as to the amount of stenosis presented, the desirable locus for the gastro-enterostomy, and whether a gastro-enterostomy, a gastropasty, gastrorrhaphy, or a gastrogastrostomy is indicated. Röntgen examination is often the means of sparing a patient the shock of an exploratory operation in cases of cancer so far advanced that successful removal would be impossible, although the clinical history reveals only slight symptoms. Postoperative röntgen-ray examinations are of great value in discovering whether the food leaves by the anastomosis or by the natural path, whether or not an hour-glass contraction has been relived by operation, and whether subsequent stenosis, or adhesions have formed. Such postoperative diagnosis will do more to check up the efficiency of an operation on the gastro-intestinal tract than any other single method of examination, and incidentally may revolutionize certain modes of surgical procedure.

In a brief way I have attempted to call attention to the röntgen method of visualizing lesions, the diagnosis of which has been particularly difficult heretofore. It takes us one step away from the art of medicine toward the science of medicine. Many patients who have been complaining of indefinite symptoms, and have sought relief for many years with indifferent success, have been examined by the röntgen method with most gratifying results to all concerned. A physician can have no patients more grateful than those who have suffered for a long time and whose difficulties have been at last actually visualized and definitely diagnosed. I may say that it detracts nothing from but rather adds to the prestige of the medical adviser or surgical consultant if he has the reputation of obtaining the fullest possible understanding of a case before deciding upon any radical course of procedure, and the physicians and surgeons who have used the röntgen method of diagnosing gastric lesions are its strongest advocates.

CONCLUSIONS. 1. The röntgen method is the most accurate and at the same time the most expensive single method of diagnosing gastro-intestinal lesions. It is also the safest and most valuable to the patient.

2. A preoperative röntgen examination in abdominal cases (*a*) will save many a case from the shock of an exploratory operation; (*b*) should shorten the time consumed at the operation; (*c*) should improve surgical statistics.

3. An exploratory operation for diagnosis is usually evidence of inadequate röntgen methods.

4. A postoperative röntgen examination of abdominal cases will lead to important modifications in the technique of such operations, just as post-treatment röntgen examination of fractures has modified general surgical methods.

5. The subject can scarcely be summarized more tersely than has been accomplished by Schmieden, who says with both wisdom and moderation: "A scientific diagnostician will not diagnose gastric lesions on röntgen-ray examinations alone, nor should he diagnose important gastric lesions without using the röntgen rays."

FURTHER OBSERVATIONS ON DIASTOLIC AND PULSE-PRESSURE.

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IN former papers^{1 2 3} attention has been called to the methods of estimating blood-pressure, and it has been demonstrated that the auscultatory method of Korotkow is the simplest and also the most satisfactory and accurate method for general use.

It must be understood at the outset that the series of tones heard over the normal brachial artery just below the arm-cuff when the pressure is gradually reduced are clear-cut only over normal vessels or vessels only slightly sclerosed, and depend upon the heart force as well as upon the state of the vessel wall, the pressure exerted by the bell of the stethoscope, the keenness of the operator's ear, etc. When the heart is irregular in force and rhythm it becomes impossible to make accurate observations at systolic or at diastolic pressure. It seems best to take the average reading between the point where the strongest beat is heard and the point where practically all beats are heard as the systolic pressure. The diastolic is best taken at the point where no sound is heard except the occasional sound produced by an excessively strong beat.

Even in certain cases seemingly normal the tones are not always clear-cut, the second may be so short that it is lost, the first may not be heard as a clear tone, but a click with a murmur may be the first sound heard. However, by reducing the pressure very slowly in such cases it is very rare in regularly beating hearts with uniformity in the force of the beats to miss the normal sequence of sounds.

The first audible sound occurs at systolic pressure. We have

¹ Warfield, L. M. The Auscultatory Blood-pressure Phenomenon: A Preliminary Report on the Clinical Determination of Diastolic Pressure, *Interstate Med. Jour.*, 1912, xix, 856.

² Warfield, L. M. Studies in Auscultatory Blood-pressure Phenomena; I. The Experimental Determination of Diastolic Pressure, *Arch. Int. Med.*, 1912, x, 258.

³ Warfield, L. M. II. The Clinical Determination of Diastolic Pressure; *Jour. Amer. Med. Assoc.*, 1913, lxi, 1254.

shown both experimentally and clinically that the diastolic pressure is to be read at the sudden transition of the third clear tone to the dull fourth tone and not at the disappearance of all sound.

Recently, Hooker⁴ has attempted to prove that the diastolic reading should be taken at the disappearance of all sound, and he lays the burden of proof on those who believe that the transition between third and fourth tones (fourth phase) is the correct point. Practically it makes but little difference in many cases, as the two phases are not more than 4 mm. or at most 6 mm. apart. But it does make some difference in other cases where the difference amounts to from 12 to 16 mm. or even more.

It is sometimes difficult to differentiate precisely the transition between the sharp and the dull sounds. A sudden lessened amplitude of the dial hand or lessened oscillation of the mercury column in cases such as this is synchronous with the change in tone. It is still more difficult to limit the disappearance of all tone, the point where some still read the diastolic pressure. Even after all tones have actually ceased the strained attention of the operator is apt to produce after-tones in the ear, which are not to be differentiated from the tones which are gradually heard to disappear. In many cases it is practically impossible to state definitely the exact point where sound ceases to be heard.

Moreover, as Goodman and Howell⁵ showed (and we have repeatedly confirmed their observations), the fourth tone persists in aortic insufficiency even to the zero of the scale. Such persistence, indeed, is pathognomonic of aortic regurgitation. Now if the diastolic is taken at the disappearance of all sound and the sound does not disappear at all, then, according to some, there can be no diastolic pressure in aortic insufficiency. Diastolic pressure measures peripheral resistance. Therefore there is no peripheral resistance according to Hooker and others. That on the face of it is impossible. Either the method is wrong or this class of cases is exceptional and must have special rules to govern it. On the other hand, to take the diastolic pressure at the fourth phase leaves no exceptions to be explained away.

Taussig and Cook⁶ have shown that in cases of aortic insufficiency it is not difficult to make a differentiation of third to fourth tones, and should confusion arise, it may be overcome by listening over the artery while the pressure is below diastolic pressure, and then gradually increasing the pressure in the cuff, a dull tone suddenly gives place to a clear, loud tone. One then reads the diastolic pressure at this point. It would appear then that until

⁴ Hooker, D. R., and Southworth, J. D. Interpretation of the Auscultation Blood-pressure Sounds, *Arch. Int. Med.*, 1914, xiii, 384.

⁵ The Auscultatory Blood-pressure Phenomenon, *Univ. Penna. Med. Bull.*, 1910, xxiii, 469.

⁶ The Determination of the Diastolic Pressure in Aortic Regurgitation, *Arch. Int. Med.*, 1913, xi, 542.

better evidence is offered, we should read the diastolic pressure at the fourth phase.

The stress laid upon this point is important, for the reason that only by having fixed points for the estimation of maximum and minimum pressures can we determine the pulse pressure. Moreover, the conviction is growing that it is the height of the diastolic pressure rather than that of the systolic pressure that is the really vital point in blood-pressure estimations.

In order for the heart to carry on the circulation it must do a certain amount of work before it succeeds in overcoming the resistance at the aortic valves. This amount of work is represented in figures as a force required to raise a column of mercury 80 to 90 mm. This is actually dead weight, which the heart must always raise before it begins to throw blood into the aorta. From the time that the aortic valves open, the force over and above that required to open the valves is used actually (making allowance for the force dissipated in distending the arch of the aorta) to keep the blood in circulation; so that the real head of pressure forcing the blood to the periphery is represented by the force exerted from the time of opening of the aortic valves to the end of systole. In other words, the diastolic pressure measures the peripheral resistance and the pulse-pressure measures the actual head of propulsive force in the arteries at the base of the heart.

Almost everyone who has written on the subject of hypertension has measured only the maximum force of the heart, the systolic pressure, and neglected the important minimum force, the diastolic pressure. Even so excellent an observer as T. C. Janeway,⁷ in a recent detailed article on "A Clinical Study of Hypertensive Cardiovascular Disease," has nothing to say of diastolic pressure, but bases all of his statistical data upon systolic pressure. While much that is of great value is given it seems that an important part of the picture has been omitted. It is as if one based statistics of anemia upon the count of the red cells alone without estimating the hemoglobin.

Hypertension is, after all, a physiological response on the part of the organism in order to maintain the circulation in equilibrium in the face of conditions which tend to produce vasoconstriction in large areas and, therefore, tend to deprive these areas of blood. That there must be some substance in the blood-stream which causes this constriction seems certain. What it is is not at present known. Recently, Voegtlin and Macht* have isolated a crystalline substance from the blood of man and other mammals which they regard as a lipoid and closely related to cholesterolin. This substance was recovered by them from the cortex of the adrenal gland. This

⁷ Arch. Int. Med., 1913, xii, 755.

* Isolation of a New Vasoconstrictor Substance from the Blood and the Adrenal Cortex, Jour. Amer. Med. Assoc., 1913, lxi, 2136.

becomes of added interest in the light of observations made by Gubar (quoted by Voegtlin and Macht). He noted "that the vasoconstricting properties of blood-serum vary in different pathological conditions, being increased in nephritis, for instance, and diminished in others." In some experiments made in the summer of 1913, we found there was no marked difference in the anaphylactic shock produced in half-grown rabbits by the injection of normal and uremic blood-serum. As lipoids do not cause anaphylaxis there should be no difference in the reaction of normal and uremic sera unless in one there was some form of proteid not in the other. This does not seem to be the case. The presence of something in the circulation, therefore, produces constriction of vessels. This calls for more force in contraction on the part of the heart. This substance may be of lipoid nature. The continued presence of this hypothetical substance naturally would lead to hypertrophy of the heart. The actual fact is that only in cases of chronic contracted red kidney does one see the pure type of left ventricular hypertrophy.

It may be affirmed that usually hypertension is accompanied by a marked increase in pulse-pressure, the pulse-pressure at times equalling the number of millimeters in normal systolic pressure. Moreover, this increased pulse-pressure seems to be absolutely essential to the maintenance of circulatory equilibrium. The hearts of the cases of cardiorenal disease are not only hypertrophied, but the cavities of both ventricles are dilated, and therefore contain and throw out more blood at every systole than a normal heart propels. It would appear that volume output and pulse-pressure are closely related. Dawson, some years ago, stated that the product of the pulse-pressure times the pulse rate represented the volume output of the ventricles in a unit of time. Erlanger⁹ later argued that this could not be correct except in certain conditions. The factors entering into the conditions giving rise to the figures of pulse-pressure and pulse rate were too many and varied to be reduced to a simple formula. There can hardly be room for dispute, however, that large pulse-pressure is associated with increased volume output when one sees the hearts at autopsy. The arch of the aorta is always much dilated also, probably to accommodate in part the excess of blood thrown out at every cardiac systole. Barach¹⁰ has recently called attention to a formula for estimating heart force. He holds that the pulse rate should be taken into consideration, for a heart with systolic pressure of 140, diastolic of 90, pulse rate of 120 is, in a unit of time, doing twice as much work as a heart with similar blood-pressure

⁹ Erlanger, J. and Hooker, D. R. An Experimental Study of Blood-pressure and of pulse-pressure in Man, Johns Hopkins Hosp. Rep., 1904, xii, 145.

¹⁰ The Energy Index. Cardiovascular Energy as Indicated by the Arterial Pressure per Minute, Jour. Amer. Med Assoc., 1914, lxii, 525.

but only 60 pulse rate. He therefore multiplies the systolic and diastolic pressures by the pulse rate, adds the two and takes the first three figures of the result as an index of work done by the heart. Reviewing my cases we cannot altogether agree with his conclusions, yet we believe that his suggestion is more valuable than any thus far proposed.

The great difficulty in estimating the value of pulse-pressure determinations is that we have no standards of normal in the various decades in men and women. For systolic pressure we have a mass of data. We are taking for pulse pressure the figures supplied by Erlanger¹¹ as standard. These are based on a large number of observations on a very few individuals, adult male medical students. Obviously such figures are not necessarily normal for the community at large. However, we think we are safe in stating that for normal adults the pulse-pressure should be 40 to 45 mm. Hg. Variations in the pulse-pressure in different diseases and in the same disease at different times are great and not always easy to interpret at their true values.

We have gone over some of our cases at the Milwaukee County Hospital. Of forty-nine cases of myocardial insufficiency at all ages the average pulse-pressure was 40 mm. The highest was 70, the lowest 15 mm. We have seen cases of myocardial disease with normal blood-pressure figures, five minutes before death. This is, however, most unusual. In 75 cases of chronic nephritis the average pulse-pressure was 62 mm. The ages of the patients ranged from ten to eighty-two years. The highest pulse-pressure, 130 mm., occurred in this group in a man, aged fifty-five years. One case, a child, aged ten years, had at one period of her stay in the hospital systolic 186, diastolic 154, pulse-pressure 32. She left the hospital improved and with 130, 80, 50 as her pressure. The most consistent low pulse-pressure were in the advance cases of pulmonary tuberculosis. This is just what one would expect. Also in typhoid fever during the third, fourth, and fifth weeks, when the fever lasts that length of time, the whole pressure picture is reduced, but the pulse-pressure is reduced relatively more than diastolic pressure.

We have taken for low pulse pressure any below 30, for high any above 50. At present it would seem that we are justified in making certain generalizations.

The pulse-pressure in aortic insufficiency is always large; in fact, it is usually the largest in any disease. In chronic nephritis the pulse-pressure is always high in the compensation stages. In some forms of arteriosclerosis the pulse-pressure is high. In myocardial insufficiency it varies. If the heart is large there is increased pulse-pressure, if the heart is small there is decreased or normal pulse-pressure. In pulmonary tuberculosis the pulse-

¹¹ Loe, cit.

pressure is low in the advanced cases. In the early cases the blood-pressure picture, as a rule, is normal or generally decreased. If the heart is large naturally the blood-pressure picture takes on more the form of that in cases of enlarged heart with general depression of the blood-pressure picture. In the acute fevers the pressure picture in the initial stages shows no particular changes. As the cases develop the whole pressure picture as a rule shows a general depression and a low pulse-pressure usually means a badly diseased heart and is an unfavorable prognostic sign.

In general when the systolic pressure is normal, increased pulse-pressure signifies peripheral dilatation. When the systolic pressure is high the increased pulse-pressure is to be regarded as normal and has no special significance. Decreased pulse-pressure or even normal pulse-pressure means marked peripheral constriction, and is, therefore, an unfavorable prognostic sign.

With low systolic pressure increased pulse-pressure occurs in practically only one condition, aortic insufficiency.

With normal systolic pressure gradually decreasing pulse-pressure usually means cardiac failure. The condition is seen often in the later stages of the high systolic increased pulse-pressure cases.

With low systolic pressure decreased pulse-pressure usually means general cardiac weakness, as seen in febrile conditions or in convalescence from long illnesses or in cachexia of malignant disease.

A CENTRIFUGE METHOD TO PROVIDE A UNIFORM STANDARD FOR WASSERMANN READINGS.

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IMMEDIATELY following its introduction as a diagnostic measure the Wassermann reaction was received with acclaim as a scientific test giving 100 per cent. average, but owing to the failure of laboratory reports to check up with the clinical findings in certain cases or owing to the failure of various laboratory workers to arrive at the same end reaction in a given case, when using the same specimen of serum, owing to laboratory reports remaining positive in various degrees longer than the clinician thought was commensurate with the amount of treatment, and many other such factors gradually led to a feeling of adverse criticism against the specificity of the Wassermann reaction, a feeling varying from a mere suspicion to an outspoken disbelief in its reliability as a laboratory procedure.

During this period there have been introduced various modifications of the original technique. Some of these modifications were designed to simplify the original method; others made a radical change in the character of the reaction, as in the substitution of the antihuman hemolytic system for the antisheep hemolytic system; another modification introduced the single unit system; again the so-called Baurer modification, and still others designed to decrease the amount of time necessary for the completion of the reaction, an important factor in the life of a busy laboratory.

When it became known that the reaction would occur in the presence of certain lipoidal extracts used as antigens, equally as well as with antigens prepared from syphilitic tissues containing *Spirocheta pallida*, a death-blow was thought to have been given to the specificity of the Wassermann test. Still later it was found that non-specific lipoidal extracts, to which was added cholesterolin, became even more active in their complement-binding power. It has been urged¹ that such antigens were more delicate in detecting the presence of syphilitic antibodies and were therefore the antigens of choice to be used in following the therapeutic progress of a given case.

By other writers² it has been held that cholesterolized lipoids, granting that they were more sensitive in detecting syphilitic antibodies, nevertheless gave a certain number of non-specific reactions leading to the grave possibility of treating for syphilis a few or many individuals never afflicted with that disease. Clearly then it is better to test all serums against both syphilitic extract antigens and cholesterolized lipoidal antigens. We feel that for diagnostic purposes it is not safe to use only a cholesterolized lipid as an antigen.

And so through persevering work and out of the knowledge born from experience in testing thousands of sera, one writer after another has called attention to and eliminated sources of error, until now it may safely be said of the Wassermann reaction, even though the original claims for specificity had to be abandoned, that for purposes of practical utility as a method of diagnosis and prognosis in syphilis this reaction now occupies a sound position, rarely excelled in laboratory procedures.

It need not be emphasized that absolutely reliable reagents should be used in the way of amboceptors, complements, antigens, etc., and that absolutely clean glassware, preferably of the Jena type, cleaned without any chemical, should be used. These things are generally checked up in all first-class laboratories.

In this paper we are not attempting any radical departure from the established Wassermann reaction technique, but are suggesting a simple modification which we believe will not only increase the

¹ John Kolmer, *Pennsylvania Med. Jour.*, December, 1913; Lloyd Thompson, *Jour. Am. Med. Assoc.*, May 9, 1914, xlii, 1458.

² B. A. Thomas and R. H. Ivy, *Jour. Am. Med. Assoc.*, January 31, 1914, lxii, 363.

accuracy of the test, but will also eliminate two sources of error, which will be discussed later.

This modification in its fundamentals consists in the use of a graduated capillary centrifuge tube to which is transferred the contents of each Wassermann tube at the end of one hour's incubation and by centrifugation the amount of sheep's cells unhemolyzed in each serum reaction is determined. These special tubes are of the centrifuge type, having a total capacity of 4 c.c., and the tip of which is barometer tubing graduated in twenty divisions, each division or unit being equal to 0.0025 c.c.³



Graduated capillary centrifuge tube.

In order to make later discussion of the method more clear it seems best to introduce the protocol at this point.

PROTOCOL. *Reagents.* A. Treat sheep's blood by the usual method and make an emulsion of the thoroughly washed red cells in a 0.85 per cent. saline in a dilution 1 to 10 with a certified pipette graduated in hundredths; introduce into four centrifuge tubes 0.5 c.c. of this emulsion and add saline q. s. 2.5 c.c.

³ These tubes may be obtained through the Edward P. Dolbey Co., Philadelphia, Pa.

Centrifuge for five minutes (exactly) with a high-speed electrical centrifuge at not less than 1200 revolutions per minute. Read the amount of cells thrown down and average the amount of cells in the four tubes. This average should fall between 18 and 20 units. If not, adjust the emulsion so that it will.

B. Amboceptor prepared and standardized by the usual methods.

C. Complement. Fresh guinea-pig serum in dilution 1 to 10 saline.

D. Antigen. Prepared and standardized by usual methods.

E. Determine complement unit by titration as follows: Use eleven tubes and add to the first eight, properly labelled:

1. Increasing amount of complement (1 to 10) from 0.1 c.c. to 0.8 c.c.
2. 0.5 c.c. amboceptor representing 1 unit in proper dilution.
3. 0.2 c.c. (one unit) antigen.
4. 0.5 c.c. sheep cells 1 to 10.
5. To tube 9 add 0.5 c.c. sheep's cells, 1 to 10, and 1 unit of amboceptor.
6. To tube 10 add 0.5 c.c. sheep's cells, 1 to 10, and 1 unit of complement.
7. To tube 11 add 0.5 c.c. sheep's cells, 1 to 10.
8. To all tubes add normal saline q. s. 2.5 c.c.

Incubate for forty-five minutes in water-bath at 37.5° C. (Shake tubes thoroughly after ten- and twenty-minute incubation.)

Centrifuge contents of first eight tubes. Take for unit of complement the quantity used in the tube which shows 3 to 4 cell units of unhemolyzed cells.

Tubes 9, 10, and 11 should show a complete inhibition hemolysis.

It is not necessary, in our opinion, to titrate both the amboceptor and the complement units separately, for the two work in a definite combination in an inverse proportion, that is, as the complement unit is increased the amboceptor unit must be decreased, and *vice versa* (cf. Chart No. 1). (It is important, however, to adjust the dilution of the amboceptor so that the complement unit falls in the 0.4 c.c., 0.5 c.c., or 0.6 c.c. tubes, lower units than these being productive of disconcerting inhibition of hemolysis in the control tubes.)

F. *Test Set*. (Cf. Chart No. 2.)

I. Add to tubes in first row:

1. 0.1 c.c. suspected serum (inactivated at 55° C. for thirty minutes).
2. One unit of complement (as determined in E).
3. One unit of antigen. (N.B.—It is our custom to use at least two antigens, either of the same or different types.)
4. Normal saline q. s. 1.5 c.c.

CHART I.—DEMONSTRATING IN THE TITRATION OF THE COMPLEMENT THAT AS THE COMPLEMENT UNIT IS INCREASED THE AMBOCEPTOR UNIT MUST BE DECREASED, AND VICE VERSA. .5 C.C. SHEEP'S CELLS, 1 TO 10, = 18.7 CELL UNITS.

Tube No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Complement 1 to 10, c.c.1	.2	.3	.4	.5	.6	.1	.2	.3	.4	.5	.6	.1	.2	.3	.4	.5	.6
Ambroceptor 1 to 1000, c.c.5	.5	.5	.5	.5	.5	.25	.25	.25	.25	.25	.25	.1	.1	.1	.1	.1	.1
Sheep's cells, 1 to 10, c.c.5	.5	.5	.5	.5	.5	.5	.5	.5	.5	.5	.5	.5	.5	.5	.5	.5	.5
Saline	q. s. 2.5 c.c.																	
	Incubated for 45 min. at 37.5° C. in water bath.																	
Unhemolyzed cells, units	10.8	4.2	3.1	1.9	1.7	1.	13.8	8.5	5.9	5.9	5.9	3.6	16.9	14.9	11.8	11.8	11.8	9.0
Cells hemolyzed, units	7.9	11.5	15.6	16.8	17.	17.7	4.9	10.2	12.8	12.8	12.8	15.1	1.8	3.8	6.9	6.9	6.9	9.7

CHART II.—PROTOCOL.

	Inactivated Patient's serum, c.c.	Complement unit determined by titration, units.	Antigen, units.	Sheep's cells 1 to 10, c.c.	Saline.	Ambroceptor unit made up to 0.5 c.c.	Sheep's cells 1 to 10, c.c.	Saline.	Incubate for 45 minutes at 37.5° C. in water bath.	Incubate for 45 minutes at 37.5° C. in water bath.	Centrifuge contents of all tubes for 5 minutes at X revolutions (about 1200 per minute). Record amount of unhemolyzed cells.
Tubes in I row1	1	1	0	q. s. 1.5 c.c.	X c.c.	.5	q. s. 2.5 c.c.			
Tubes in II row1	1	0	0	q. s. 1.5 c.c.	X c.c.	.5	q. s. 2.5 c.c.			
Tubes in III row05	1	0	.25	q. s. 2.5 c.c.						
Alpha tubes	0	1	1	0	q. s. 2 c.c.	0	.5	0			
Beta tubes	0	1	0	0	q. s. 1.5 c.c.	.5	.5	0			
Reagents' control	0	1	1	0	q. s. 1.5 c.c.	.5	.5	0			

II. Add to the tubes in second row:

1. 0.1 c.c. suspected serum, inactivated.
2. One unit of complement.
3. Normal saline q. s. 1.5 c.c.

III. Add to tubes in third row:

1. 0.05 c.c. suspected serum.
2. One unit of complement.
3. 0.25 c.c. sheep cells 1 to 10.
4. Normal saline q. s. 2.5 c.c.

IV. Prepare a set of four tubes, called Alpha tubes, each tube to receive:

1. One unit of antigen.
2. One unit of complement.
3. Saline q. s. 1.5 c.c.

V. Prepare a set of four tubes called Beta tubes, each tube to receive:

1. One unit of complement.
2. Saline q. s. 1.5 c.c.

VI. As reagent control prepare one tube to contain:

1. One unit of complement.
2. One unit of antigen.
3. Saline q. s. 1.5 c.c.

Shake and incubate the foregoing tubes for forty-five minutes at 37.5° C. in a water-bath and then add to tubes under I and II:

1. 0.5 c.c. sheep's cell emulsion 1 to 10.

2. 0.5 c.c. (?) amboceptor = 1 unit except to all sera which in III row tubes show complete hemolysis, indicating presence of sufficient native sheep amboceptor. No artificial amboceptor is to be added to these sera. Sera which show partial hemolysis in III row tubes are to receive the proper fraction of the amboceptor unit.

To tubes in IV (Alpha tubes) add:

1. 0.5 c.c. sheep's cell emulsion 1 to 10.

To tubes in V (Beta tubes) and VI (reagent control tube) add:

1. 0.5 c.c. sheep emulsion 1 to 10.
2. 0.5 c.c. (?) amboceptor = one unit.

Shake and incubate all tubes (except those under III) for forty-five minutes in water-bath incubator at 37.5° C. Shake tubes again after ten minutes and twenty minutes' incubation.

G. Take readings as follows: Transfer by means of Wright's pipettes the entire contents of each of the foregoing tubes into the special centrifuge tubes, washing clean with a slight excess of normal saline:

1. Centrifugalize the Alpha tubes and average them.
2. Centrifugalize the Beta tubes and average them.

The average Alpha minus the average Beta will represent the average amount of cells hemolyzed in a negative reaction, or conversely the average number of units of unhemolyzed cells in a 100 per cent. positive serum.

3. Centrifugalize all the test and control tubes and establish the strength of reaction of each by a percentage scale. Record the readings in the following way:

Date May, 1914	No. of serum	Name	Unhemolyzed cells in Series I (front row) expressed in centrifuge units.	Unhemolyzed cells in Series II (back row) expressed in centrifuge units.	Unhemolyzed cells in front tube minus those in back or control tube.	100 per cent. for each serum is represented by alpha minus number of units in series II, or back tube.	Per cent. of cells not hemo- lyzed in sus- pected serum i. e., percent- age of positivity.
	1	A	10.8	2.4	8.4	16.4	51.2
	2	B	16.2	2.2	14.0	16.6	84.3
	3	C	11.2	4.0	7.2	14.8	48.6
	4	D	.5	.3	.2	18.5	0
	5	E	18.9	1.0	17.8	17.7	100

Alpha = 18.8

Beta = 2.8, Alpha minus Beta = 16 or an average of 100 per cent.

To determine the percentage of positiveness of each serum proceed as follows:

After centrifugation read the number of cells left unhemolyzed (to be hereafter called "cell units") in the front row tube and subtract from that the number of "cell units" in the back row tube—the control tube.

Now the average number of "cell units" of the four "Alpha tubes" minus the average "cell units" in the four Beta tubes will represent the average 100 per cent. positive for the entire reaction, the 100 per cent. here being equivalent to the absorption of one complement unit.

It is possible to establish an individual 100 per cent. for each serum in the reaction by subtracting the number of "cell units" in the serum control tube from the Alpha average. Therefore the actual 100 per cent. of each serum is easily calculated by comparing the difference in "cell units" of the serum tube and its control with the 100 per cent. established for that serum. It is quite essential to establish this 100 per cent. for each individual serum for two reasons: (1) because certain sera may contain native sheep amboceptor beyond the double unit content as determined by the Bauer modification, so that the number of "cell units" will fall below the Beta established for the reaction; (2) to eliminate errors introduced by slight anticomplementary action in certain sera in which the number of "cell units" in the control tube slightly exceeds the Beta established for the reaction.

Take, for example, that while 16 cell units represents the average 100 per cent., 14.8 cell units is the individual 100 per cent. for serum No. 3 (cf. Chart.) Now if 14.8 is 100 per cent. what is the percentage of 7.2? This is obtained by simple proportion as follows: 14.8 : 7.2 :: 100 : X.

Occasionally strongly positive sera will be encountered whose unhemolyzed cell bulk may fall a few units below the cell bulk of the average Alpha without, however, showing any evidence of hemolysis. Such sera, though falling slightly below 100 per cent. on calculation (say 98 per cent.), should, nevertheless, be considered 100 per cent. reactions, *provided* no visible hemolysis has taken place. At present we are unable to explain this phenomenon, except possibly on a theory of Kaplan regarding surface tension relations.

It will be seen by studying the protocol that in this proposed modification there is little difference from the Wassermann technique generally in use, except in the fact that at the end of forty-five minutes' water-bath incubation the material is transferred from the Wassermann tube to the centrifuge tube and after centrifugation the final reaction is read *at once*, and except that we insist upon having 3 to 4 cell units unhemolyzed in the control tubes (as already determined by the complement titration), so that we may be sure that hemolysis has proceeded as far as it can within the given limit of time. As long as this principle is adhered to the exact reading of each individual serum is under accurate control. Otherwise the technique is the one unit system, which to our view appears the most rational. We also include a tube to detect the presence, in each serum, of native sheep amboceptor, sufficient in itself to cause complete hemolysis.⁴

We agree with other writers⁵ that the presence of sufficient native sheep amboceptor occurs rather more frequently than the serologists who do not include this check on the serum are aware of. This also creates an error in diagnosis to the negative side.

Where the presence of native sheep amboceptor was not checked we frequently observed that in some sera the total amount of cells contained in the control tube was completely hemolyzed, while the Beta average was perhaps 4.2 units, suggesting that the increased hemolysis came from the excess amboceptor—and if this hemolysis occurred in the back or control tube it must likewise occur in the front or diagnosis tube.

In a similar way we may infer the presence of anticomplementary bodies in the serum when the cell units unhemolyzed in back or control tube greatly exceeds the average determined by the Beta tubes—where this occurs in sera, for diagnosis, we think it unsafe to interpret the strength of the reaction by subtracting the back tube unit from the front tube unit and prefer to request a fresh specimen of serum. That it is unsafe to interpret such sera has forced itself on us, because it has been our custom to transfer positive and negative sera from the German Hospital, where the reactions are done on Wednesdays, to be used as controls in the reactions

⁴ J. Bauer, *Deutsch. med. Wochenschr.*, 1908, xxxiv, 698.

⁵ Dexter and Cummer, *Arch. Int. Med.*, May, 1912, ix, 605.

performed at the Methodist Hospital on Saturdays, and *vice versa*, thinking that such sera would be fresher as controls after three days' refrigeration than if kept for one full week in the ice-box. The same technique and the same reagents are used at both hospitals by the same laboratory worker, and yet it occurs, not infrequently, that sera that were strongly positive at the German Hospital, when tested again as a control, three days later, had developed sufficient anticomplementary reaction as to cause 50 per cent. inhibition of hemolysis in the control tube. Therefore it is of the utmost importance to test sera within twenty-four to forty-eight hours after withdrawing the blood.

It will be noted that the final reactions by this method are made at the end of forty-five minutes' incubation when the transfer of contents from Wassermann to centrifuge tubes is made. This is to eliminate the first of the two errors referred to earlier in the paper.

This first source of error lies in the following fact: In titrating for either the complement or the amboceptor unit by the methods generally in use the tubes are incubated for one hour and the unit determined on the basis of that time interval; but in the actual serum analysis readings are made at the end of the first hour, the tubes then reincubated and read the end of the second hour, and occasionally the final reading is not made until the following day. Surely this is wrong—for it may easily be proved (cf. Chart No. 3) that in reading a titration set at the end of one hour the unit of complement may be 0.5 c.c.; but if reincubated for an hour it will be seen that hemolysis has proceeded further and that the complement unit may be 0.4 c.c., and if allowed to stand for several hours or over-night the complement unit may be even lower, 0.35 c.c. or 0.3 c.c. This is in keeping with the observation and explains the fact, that sera that are weakly positive when read at the end of one hour may have become negative if read at the end of the second hour—the usual time limit.

CHART III.—DEMONSTRATING THAT THE AMOUNT OF HEMOLYSIS DEPENDS ON THE LENGTH OF INCUBATION. 25 C.C. SHEEP'S CELLS, 1 TO 10, = 7.3 CELL UNITS.

Tube No.	1	2	3	4	5	6
Complement 1 to 10, c.c.1	.2	.3	.4	.5	.6
Amboceptor, c.c.5	.5	.5	.5	.5	.5
Sheep's cells 1 to 10, c.c.25	.25	.25	.25	.25	.25
Saline			q. s. 2 .5 c.c.			
Unhemolyzed cells, or cell units, after						
45 min. incubation	3.8	1.6	.6	.2	0	0
90 min. incubation	3.1	.7	.2	0	0	0
135 min. incubation and 6 hrs. at room temperature	2.5	.3	0	0	0	0

The second, the most important error, and the one most difficult to correct, is the element introduced by personal equation in reading the end reactions by the visual method, the one most generally in use. Given two serologists of equal skill, each using the same plan of technique and the same reagents, when the final reading is made, say at the end of the two-hour limit, by the visual method, that is by visually estimating the amount of hemolysis that has taken place and the amount of sheep corpuscles that remain unhemolyzed, one serologist may call this serum weakly positive and the other may call it a delayed negative. In other words, there may be an error approaching 25 per cent. on the part of the one or the other worker and each may think he is right. But it is severe on the clinician, who is sometimes left in doubt, and it is doubly hard on the patient. The error may approach 25 per cent. because it is customary in most laboratories to divide their scale of positiveness into four groups. Serologist A⁶ classifies his sera as follows:

++ indicates absolute inhibition of hemolysis or a positive reaction.

+ indicates anything between absolute inhibition and 50 per cent. of inhibition of hemolysis.

= indicates between 50 per cent. of inhibition of hemolysis and total hemolysis, or practically a negative reaction.

— indicates total hemolysis, or a negative reaction.

Serologist B⁷ classifies his sera as follows:

1+ or total inhibition of hemolysis.

$\frac{3}{4}$ + or where approximately three-fourths of cells are unhemolyzed.

$\frac{1}{2}$ + or where approximately one-half of cells are unhemolyzed.

$\frac{1}{4}$ + or where approximately one-fourth of cells are unhemolyzed.

0 or complete hemolysis.

Serologist C classifies his sera as follows (our former classification):

+4 or total inhibition of hemolysis.

+3 or where approximately three-fourths of cells remain unhemolyzed.

+2 or where approximately one-half of cells remain unhemolyzed.

+1 or where approximately one-fourth of cells remain unhemolyzed.

— or where complete hemolysis has taken place.

These various degrees of positiveness are then named "very strongly positive," "positive," "positive, moderately strong," "weakly positive," "delayed negative," and "negative or sharply negative."

⁶ Charles F. Craig, *Jour. Am. Med. Assoc.*, April 13, 1914, p. 1232.

⁷ John L. Laird, personal communication.

It will be seen that in the scale of Serologists B and C the difference in each degree is relative one of 25 per cent., while in the scale of Serologist A it is nearly 50 per cent.

It is in avoiding such an error of personal equation that the proposed modification has possible merit in providing a uniform standard of reading on an absolute percentage scale.

Certain sera may be sufficiently strong in syphilitic antibodies as to be capable of absorbing more than one unit of complement, so strong that it may not be until three or four full complement units have been added that the "antibody equation" has been satisfied and enough complement in excess has been left to cause total or partial hemolysis (cf. Chart No. 4). These sera, by the proposed method, can be equally well percentaged to two, three, or four hundred "per cent. positive" or fractions thereof, where absorption of each complement unit is equivalent to 100 per cent. By carrying out this procedure in all "100 per cent. positives" the clinician will be informed of the *exact strength* of syphilitic antibody content, and will therefore not be surprised that the Wassermann reaction in a given case does not become reduced more quickly from a "+4" result in the face of urgent treatment, when in reality that serum titrates to a "+8" or a "+12" positive or by our proposed scale "200 per cent. or 300 per cent. positive" or fractions thereof.

CHART IV.—DEMONSTRATING METHOD OF RECORDING RESULTS OF SERA WHICH ABSORB MULTIPLE UNITS OF COMPLEMENT. ALPHA = 17.3. BETA = 4.9.

Tube No.	Patient's serum, c.c.	Complement units.	Antigen units.	Saline, c.c.	Ambocceptor, units.	Sheep's cells 1 to 10, c.c.	Cells in front row centri-fuge units.	Cells in back row centri-fuge units.	Front minus back.	100 per cent.	Result.
1	.1	1	1	q. s. 1.5	1	.5	17.5	4.1	13.4	13.2	100
2	.1	2	1	q. s. 1.5	1	.5	17.5	4.6	12.9	12.7	100
3	.1	3	1	q. s. 1.5	1	.5	17.0	4.2	12.8	13.1	100
4	.1	4	1	q. s. 1.5	1	.5	14.4	4.5	9.9	12.8	77

Result = 377
per cent.

We urge the necessity of using small-bore pipettes throughout the reaction to insure closer accuracy, and we believe that 1 or 2 c.c. pipettes graduated in hundredths should be used for all reagents save possibly the saline. It stands to reason that in a reaction whose delicacy is checked up at so many points (*i. e.*, in the determination of the exact complementary, hemolytic and antigenic units, etc.) it is unwise to risk an error of pipettage by using a 10 c.c. pipette graduated in tenths, when even in the hands of the most expert an occasional error creeps in when filling a hundred or more tubes.

This holds with all the reagents, but most particularly with the sheep's cell emulsion, even in filling a small series of tubes, for the reason that by gravity alone an emulsion of cells in a 10, 5, or even 2 c.c. pipetted will fall toward the tip of the pipette, so that the first unit pipetted out will be richer in cells than will subsequent ones. This error will be minimized by using throughout 1 c.c. pipettes graduated in hundredths. The real extent of this error is not appreciated until one makes use of the centrifuge tubes and by centrifugation determines the difference in cell bulk or cell units (cf. Chart No. 5). Another point in this connection is to use the utmost care in homogenizing the sheep's emulsion by proper and uniform shaking so that each tube shall receive as nearly as possible the same unit of blood. To this end we have discarded the shaking of cells in a flask or graduate and at the time in the reaction when the sheep cells are to be used an assistant pours the emulsion from one beaker to another twenty times before the first pipetteful is drawn and continues such decantation until all the tubes have been filled. All these refinements of technique are time-consuming and laborious, and may be criticized from that viewpoint; nevertheless, we believe that they are essential to obtain the highest degree of accuracy.

CHART V.—DEMONSTRATING THE INCREASE IN ACCURACY IN PIPETTAGE BY USING 1 C.C. PIPETTE INSTEAD OF 10 C.C. PIPETTE.

		Cell Units.						
.5 c.c. sheep's cells, measured with	10 c.c. pipette	20	24	19.9	21	21.2	20.7	21.2
	Greatest difference = 4.1 units.							
	1 c.c. pipette	20.1	20	19.9	19.6	19.7	19.7	19.4
	Greatest difference = 0.7 unit.							

It may be urged against this proposed method that the total time for performance of the reaction will be lengthened. This is not so. On the contrary there is an actual shortening of the total time limit together with an increase in accuracy. The only reason why the two-hour limit is imposed for final readings by the visual method is to permit of the sedimentation by gravity of the unhemolyzed cells, and even at the expiration of this time limit only the completely hemolyzed (or negative) tubes and those showing total inhibition of hemolysis (the positive sera) can be accurately read and the others may have to stand twelve hours or more in the refrigerator before they can be safely estimated by the visual method, and even here the error of personal equation enters. Twenty-five serum reactions may be transferred from Wassermann tubes to centrifuge tubes, centrifuged, read, and recorded in percentage nomenclature within sixty minutes' time. This has been

repeatedly checked in our hands and that, too, when we have had only sixteen centrifuge tubes at our disposal.

As regards the cleaning of the capillary end of the tube the difficulty is easily overcome by using a Wright pipette attached to the water faucet by a length of rubber tubing and the stream of water conducted directly into the capillary end of the centrifuge tube. After use the tubes are all thoroughly washed at once, dried in the sterilizer, and before using again are thoroughly rinsed with fresh 0.85 per cent. saline. When properly cared for these tubes are not as fragile as they look, as witness the fact that our sixteen tubes have been in use for weeks without a single tube mortality.

The only valid objection to this method lies, possibly, in the cost of the tubes, our original set costing one dollar each, but we are assured by the glass manufacturers that such tubes, prepared from Jena glass and certified may be bought in bulk for fifty cents each, or possibly less. Sixteen centrifuge tubes will be found sufficient in those laboratories where the number of sera to be tested does not exceed twenty-five.

In passing we wish to put on record the observance of the following phenomenon, namely, that in titrating the complement unit with 0.25 c.c. of 1 to 10 sheep's corpuscle emulsion (which is equivalent to 0.5 c.c. of 1 to 20 emulsion) we may find that 0.5 c.c. is the "complement unit" (*i. e.*, the smallest amount of complement which, with a given unit of hemolysin, will cause complete hemolysis of 0.25 c.c. of 1 to 10 sheep's cells); we also found that this same amount of complement, namely, the 0.5 c.c.=1 unit, when used with the same amboceptor unit was capable of hemolyzing almost double the amount of sheep's corpuscles, namely, 0.5 c.c. of 1 to 10 emulsion (cf. Chart No. 6).

CHART VI.—0.5 C.C. SHEEP'S CELLS=17.2 CELL UNITS. 0.25 C.C. SHEEP'S CELLS=8.5 CELL UNITS.

Tube No.	1	2	3	4	5	6	7	8
Complement 1 to 10, c.c.	.5	.6	.7	.8	.5	.6	.7	.8
Amboceptor 1 to 2000, c.c.	.5	.5	.5	.5	.5	.5	.5	.5
Sheep's cells, 1 to 10, c.c.	.25	.25	.25	.25	.5	.5	.5	.5
Saline	q. s. 2.5 c.c.							
Incubated for 45 min. at 37.5 ° C. in water bath.								
Unhemolyzed cells, units	.4	.2	.1	0	4.2	2.9	2.7	2.3
Hemolyzed cells, units .	8.1	8.3	8.4	8.5	13.0	14.3	14.5	15.5

REVIEWS

BLOOD-PRESSURE IN MEDICINE AND SURGERY. A GUIDE FOR STUDENTS AND PRACTITIONERS. By EDWARD H. GOODMAN, M.D., Associate in Medicine in the University of Pennsylvania. Pp 226; 57 illustrations. Philadelphia and New York: Lea & Febiger, 1914.

THIS little volume on blood-pressure, written by one who has always been an interested student of the subject, as well as one of the first to emphasize the value and possibilities of the auscultatory method of determining blood-pressure, must be regarded as one of the most useful of the several books on blood-pressure that have appeared recently. The value of the book lies in the fact that its author has furnished a decidedly practical treatise without neglecting the scientific aspects of his subject.

The first two chapters briefly describe the essential facts which govern the physiology of blood-pressure. This is followed by a short historical sketch and a description of the better known instruments that have been devised for the clinical estimation of blood-pressure. In accordance with the best recent authorities, Goodman regards mercury instruments as the more reliable, and for practical purposes, rather favors the new Nicholson sphygmomanometer.

The auscultatory method of determining blood-pressure, rightly regarded by the author as the only reliable method, is discussed in detail. However, he does not attempt to settle the disputed question as to just what point marks the diastolic pressure.

He discusses with considerable care physiological variations in blood-pressure before taking up its pathological changes. Permanent hypertension, he believes, is met with in but two groups of cases; the so-called cases of simple hypertension (hyperpiesis of Allbutt) and in nephritis. With considerable reason, Goodman suggests that perhaps in their final analysis all cases of permanent high-pressure will fall into the latter group. He definitely excludes arteriosclerosis *per se* as a cause of high blood-pressure, a fact which he emphasizes later on when describing that disease. After considering hypotension, he takes up in detail the blood-pressure changes that occur in various cardiovascular diseases and diseases of the blood. His views on the so-called cardiac neuroses are illustrated by personal observations. At this point he digresses somewhat to discuss various functional cardiac tests.

The chapter on blood-pressure in renal conditions includes a good review of the various theories of hypertension in nephritis.

In the chapter on blood-pressure in acute and chronic infections, Goodman summarizes some interesting observations which he made on 25 cases of pneumonia, from these he concludes that a fatal outcome in this disease does not always accompany a blood-pressure lower than the pulse rate, nor does he believe that a pressure higher than the pulse rate invariably mean ultimate recovery. After taking up blood-pressure in various nervous diseases, in obstetrics, in anesthesia, in certain surgical conditions and complications, as shock, hemorrhage, etc., he briefly mentions blood-pressure changes in some conditions of the gastro-intestinal tract, in diseases of the ductless glands, and in ophthalmology. The final chapter details in a wholly admirable manner the various therapeutic measures that are available for the management of both hyper- and hypotension.

Although a book of this kind must of necessity be based to a large extent upon work that has previously been done by others, in this volume the author's views and the results of his personal experiences are frequently encountered. Needless theoretic discussion has been avoided. Goodman has adhered closely to his subject, and as a result has given us an eminently practical book which can unreservedly be recommended, and which should form a useful addition to the library of both the practitioner and the medical student.

G. M. P.

MILITARY HYGIENE. By FRANK R. KEEFER, A.M., M.D., Lt.-Colonel Medical Corps, United States Army; Professor of Military Hygiene, United States Military Academy, West Point. Pp. 287; illustrated. Philadelphia and London: W. B. Saunders Company, 1914.

IN this manual the author is clear, compact, and comprehensive, and shows that in the care of troops not the cure but the prevention of disease is paramount, and the officers to be really efficient, "Must add to the qualities of courage and firmness those of nurse, monitor, and purveyor for grown-up children in whom the bumps of providence and destruction are abnormally developed." The point that the character, mental, and nervous condition should be most carefully investigated at the time of enlistment is well taken.

The chapter on physical training is excellent: "'tis not a soul, 'tis not a body we are training, but a man, and we must not divide him." The interrelation between intellectual and physical functions is well shown. Physical training is well classified and military physical training analyzed, emphasis being laid on the fact that

activity, agility, and smartness rather than mere strength are desired, and that overdoing is not rectifiable. Preventable diseases are clearly and concisely treated, particularly typhoid and typhoid vaccination.

The subject of water is gone into thoroughly and the different methods of purification described, with the conclusion that if there is any doubt as to the purity, always boil. The discussion of foods and their preparation furnishes an excellent summary of the facts known concerning food values, with useful suggestions.

Sanitation of posts and barracks and of marches, camps, and battlefields is thoroughly covered, and disposal of waste is discussed in detail. Service in the tropics and in the arctic region is considered at length, and nostalgia and homesickness is recognized.

The chapters on venereal diseases, alcohol, and narcotics are admirable. Facts are presented in a frank, scientific, and conclusive way, and logical conclusions are self-evident: truly, "It is in the conscience of the young man that prophylaxis should begin."

T. G. A

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by HOBART AMORY HARE, M.D., Professor of Therapeutics, Materia Medica, and Diagnosis in the Jefferson Medical College, Philadelphia, etc., assisted by LEIGHTON F. APPLEMAN, M.D., Instructor in Therapeutics in the Jefferson Medical College, Philadelphia, etc. Vol. II. June. Pp. 460; 111 illustrations. Philadelphia and New York: Lea & Febiger, 1914.

THE June issue of *Progressive Medicine* is always an interesting and instructive volume, particularly to the surgeon. The important subject of hernia is dealt with by William B. Coley in 54 pages. John C. A. Gerster then follows with a comprehensive review of the surgery of the abdomen exclusive of hernia. As usual, surgical affections of the stomach and duodenum come in for a large share of his attention, although the intestines and, to a less extent, the liver and pancreas are by no means neglected. Another noteworthy contribution to this volume is John G. Clark's excellent review of recent advances in gynecology. Cancer of the uterus, the value of roentgen-ray treatment in various uterine conditions, and gonorrhea in the female are the subjects discussed at greatest length. To the internist, Alfred Stengel's article on diseases of the blood, diathetic and metabolic diseases, diseases of the thyroid gland, nutrition, and the lymphatic system, should prove profitable reading. With rare good judgment this author has emphasized

all the best work that has recently been done in these always important subjects. The concluding section of the volume is Edward Jackson's review of ophthalmology in which he adequately covers all the structures of the eye, while devoting particular attention to glaucoma and cataracts.

G. M. P.

THE PRACTITIONER'S VISITING LIST FOR 1915. Pocket size; bound in leather with flap. Pp. 192. Philadelphia and New York: Lea and Febiger, 1914.

THE *Visiting List* for 1915, which has just appeared, will be welcomed by the many practising physicians who year after year come more and more to depend upon this helpful and convenient little book. Thirty years of experience has enabled the publishers to produce the most complete and practical pocket visiting list obtainable. In addition to a simple yet accurate method for keeping the record of daily calls, the book contains much useful data accessibly arranged, which cannot fail to appeal to any busy practitioner. Tables of weights and measures, incompatibilities, methods of urine examination, poisons and antidotes, an adequate table of doses, besides pages for addresses, birth and death records, cash account, and general memoranda are some of the praiseworthy features of this visiting list.

G. M. P.

THE OCCUPATIONAL DISEASES: THEIR CAUSATIVE SYMPTOMS, TREATMENT, AND PREVENTION. By W. GILMAN THOMPSON, M.D., Professor of Medicine, Cornell University Medical College in New York City. Pp. 724; 118 illustrations. New York and London: D. Appleton & Co., 1914.

It is a remarkable truth that there has never heretofore been published in this country a book dealing with the occupational diseases. That such a book has long been required is well known, but until the appearance of the present volume investigators and others interested in these disorders have had to depend upon the isolated monographs and reports that have appeared from time to time dealing with but one or two of the numerous disorders that arise directly as a result of the occupation of the individual. In European countries numerous treatises have appeared upon this subject, and while they have more or less bearing upon the American phases of the problem of occupational hygiene, still there has long been needed a reference-book which specifically discusses from the American point of view industries of this country, variations in the

working conditions, and the difference in the employees as contrasted with the European standards. Such a book would be of value not only to the physician but also to the sociologist and the philanthropist, to the members of State Legislatures, and to the officers of insurance companies. To meet this need, Dr. Thompson, long an investigator and student of occupational diseases has prepared the present work. Written from the stand-point of a physician, largely for physicians, the book, on account of the broad view of the subject taken by the author, will adequately meet the requirements of those interested in the occupational disorders from other stand-points.

The book is divided into seven parts: Part I deals with the whole subject in general and with the pathology and etiology of the diseases resulting from occupational risks in particular. Part II considers the prevention of occupational disorders in general and the treatment of the more important diseases in detail. Part III, the longest of the several divisions, treats of the various toxic and irritant materials which may cause injury to those working with them. The mode of preparation and the use to which they are put in manufacturing other products are first detailed, then follow the symptoms produced by them, the prevention of injury, and the treatment. The diseases due to harmful environment, such as compressed and confined air, extremes of heat and cold, excessive light, and electric shocks are to be found in Part IV. The result of harmful occupations upon the various parts of the body, as the eyes, the ears, the blood, and the skin, are fully diseussed in Part V. Part VI is a short chapter upon the influence of alcohol, syphilis, the abuse of foods, non-alcoholic stimulants, drugs, and tobacco on the occupational diseases. In Part VII are collected the various occupations from which injuries or diseases may occur to those engaged in them. In addition there are to be found five appendices which condense much of the earlier material into tabular form.

From this brief outline of the contents of the book it can be readily seen how carefully and thoroughly the whole subject of disease arising from occupation has been dealt with. The author treats his subject with skill and with knowledge. He brings to bear upon occupational diseases the fruits of extensive study, not only by himself but also by those who have investigated various industries and the injuries arising from them, so that he has compiled a book which is broad and many-sided, and hence of value as a text-book. The present volume is terse, clearly written, and most interesting. It would manifoldly repay the average physician to read and to learn of the many ramifications and diverse courses that diseases due to occupations take. Numerous obscure lesions may be traced to occupation, and the relief of them will be found in the removal of the apparently remote cause, not before then. Dr. Thompson teaches a most pertinent lesson; the need of a careful,

well-taken history of the patient's mode of working, character of work, and conditions under which he works. If this alone were the lesson of the book the author could feel that he has succeeded in his undertaking.

J. H. M., JR.

TEN SEX TALKS TO BOYS TEN YEARS AND OLDER. By IRVING DAVID STEINHARDT, M.D., Instructor in Clinical Surgery and Assistant Surgeon, Cornell University Medical School; Assistant Pediatricist, Mount Sinai Hospital, New York City, etc. Pp. 187; 12 illustrations. Philadelphia and London: J. B. Lippincott Co., 1914.

THESE talks, now somewhat revised and enlarged, were originally presented before several social and educational societies in New York and Brooklyn, and were later published in *Pediatrics*. After describing rather vividly the anatomy and physiology of the male sexual organs, and supplementing the descriptions with illustrations, the author discusses in a quite loose general sort of way the sexual diseases and habits, their dire consequences, and means of avoiding them. He then considers the duties and obligations of husbands and fathers, and in a final chapter gives his ideas about babyhood. Throughout the book Steinhardt emphasizes the fact that the sexual relation is unnecessary, and he strives with much earnestness and some success to inspire a more wholesome respect on the part of the reader for the sex of his "mother, sister, wife, or daughter." As stated in the preface, "no attempt is made to be scientific but only to speak plainly." After reading the book the query naturally arises, if such plain speaking does not arouse a morbid curiosity in young boys which only experience can satisfy. If, however, it is ever wise for boys to learn of such things from books, this book may be recommended.

T. G. M.

MANUAL OF OBSTETRICS. By EDWARD P. DAVIS, A.M., M.D., Professor of Obstetrics in the Jefferson Medical College, Philadelphia. Pp. 463; 171 illustrations. Philadelphia and London: W. B. Saunders Company, 1914.

THE opening chapters deal with the anatomy and physiology of the pelvis, including a short description of abnormal pelvis and the development of the embryo. The section on pregnancy includes chapters on the diagnosis, hygiene, physiology, and pathology of pregnancy. The various toxic conditions of the pregnant woman are fully considered, and the author emphasizes the advantage of

hospital care for such cases. Dystocia of both maternal and fetal origin is clearly explained in the chapter on pathological labor. All forms of hemorrhage occurring in pregnancy, labor, and the puerperium are discussed at length, favorable comment being made on the treatment of placenta previa by Cesarean section. A good description of puerperal septic infection is included in the chapter on the pathology of labor. Part IV deals with the normal puerperium, the care of the normal infant, and concludes with a chapter on obstetric asepsis and antisepsis. Obstetric surgery in its various forms is discussed in Part V. The newer extraperitoneal section of the pregnant uterus and the advantage of this operation in presumably infected cases, and the enlargement of the pelvic inlet by resection of the sacral promontory, are mentioned. The next chapter takes up rupture of the uterus, already fully described under the pathology of labor. The morbid conditions of the fetus and infant are discussed in the concluding section. The first chapter is devoted to the medico-legal aspects of obstetric practice, a clear statement of responsibilities and liabilities occasionally to be encountered.

The omission of theoretical discussion, the clear style of description, and the definite directions as to treatment combine to form a valuable practical book.

P. F. W.

ORTHOPEDECS IN MEDICAL PRACTICE. By PROF. ADOLF LORENZ, Director of the Imperial University Ambulatorium for Orthopedic Surgery in Vienna, and DR. ALFRED SAXL, Assistant Surgeon in the Imperial University Ambulatorium for Orthopedic Surgery in Vienna. 39 illustrations. New York: William Wood & Company.

"THERE exists a more intimate connection between internal medicine and orthopedic surgery than at the first glance might appear to be the case." "Under the eyes of the physician, the early subtle symptoms of many congenital and nearly all acquired deformities may be easily overlooked."

These sentences are the opening statements in the preface of Lorenz and Saxl's book. The phrase, "intimate connection" should also strongly imply intimate relationship, especially in the developmental stage of deformity producing disease. The fact that incipient conditions, which later on in the life of the individual produce deformities, may be overlooked, makes the correct diagnosis of the disease of the most vital importance. The chief alleged mission of this book is to aid the general practitioner in the making of such an early diagnosis. Physicians who need such a book are obviously those practitioners, in both country and city, who have not the time or opportunity to become proficient in orthopedic

science and who need a clear, concise, brief outline of symptoms which will lead them at once to the proper diagnosis, and will show them the cases which are grave and in which immediate treatment is of vital importance; these physicians should be aided in such a manner that they will be able to institute the proper early treatment when it will most benefit the patient.

The first chapter of Lorenz and Saxl's book deals with diseases of the respiratory system, the second chapter, with diseases of the circulatory system, the third chapter, with diseases of the digestive system, the fourth chapter, with diseases of the urinary system, the fifth chapter, with diseases of the nervous system, and the sixth, with diseases of the locomotor system. But, comparatively little is given, and that is not sufficiently emphasized, relative to the complex and subtle manifestations of early symptoms. The bulk of the substance of this work is a discussion of treatment of deformities due to disease, many of which deformities result from the lack of early diagnosis or improper treatment or both. It is the reviewer's opinion that this book will be of little service to the general practitioner.

W. J. M.

THE HISTORY OF RHINOLOGY FROM ITS INCEPTION TO THE EIGHTEENTH CENTURY. (Geschichte der Nasenheilkunde von ihren anfangen bis zum 18 Jahre hundert.) By KARL KASSEL, M.D. Pp. 476. Wurtzburg: A. Steubers Verlag, 1914.

THIS voluminous work of 476 pages comprises a detailed history of this branch of specialism as set forth in the title.

Part I embraces rhinology as practised by the ancients (Egyptians, Assyrians, Babylonians, Jews, and East Indians). This data is derived principally from old papyri and the works of Herodotus, and consists chiefly of excerpts dealing with the crudest methods of treatment. The rhinological knowledge of ancient Greece is culled from the works of Hippocrates and Galen, while Celsus, Cato, and others are the authorities for the Romans. Part II deals with rhinology of the Middle Ages, each author of note being quoted usually *in extenso* and very often in the original language (Latin or Greek). Part III begins with Paracelsus and continues to the end of the sixteenth century. Part IV comprises the seventeenth century and includes the work of many writers, bringing the book up to the beginning of the eighteenth century.

This monograph is most elaborate in its conception, and at once impresses the reader with the immense amount of reference work required by the author for its compilation. The style is distinctly German, that is, tiresome in its thoroughness and detail; however, as a work of reference for one interested in this topic, it bids fair on its completion to be the standard for all time.

G. M. C.

MODERN PROBLEMS OF BIOLOGY. By CHARLES S. MINOT, S.D., LL.D., Professor of Comparative Anatomy, Harvard University Medical School. Pp. 124; 53 illustrations. Philadelphia: P. Blakiston's Son & Co.

THE six lectures which Professor Minot delivered at Jena, as exchange professor, are here presented in book form. In his preface the author comments that "it is always a difficult problem to so present new biological discoveries that they will be comprehensible to a mixed public and yet lose nothing of their scientific value." The masterly way in which this obstacle has been surmounted is indeed remarkable. No easy task when the titles of his lectures are reviewed: (1) the new cell doctrine; (2) cytomorphosis; (3) the doctrine of immortality; (4) the development of death; (5) the differentiation of sex; (6) the notion of life.

That there has been no confusion of fact with fancy or overlapping of the known and unknown has made this possible. An honesty to confess ignorance, where such exists, has added weight to and placed in their proper perspective his statements of facts.

A. A. H.

THE SURGERY OF THE STOMACH. By HERBERT J. PATERSON, M.A., M.C., M.B., F.R.C.S. Second Edition. Pp. 334; 83 illustrations. New York: William Wood & Co., 1914.

THIS, the second edition, shows no exceedingly marked revision of its first. However, there are many additions and improvements added in the text and in the illustrations. Some of the photographs have been reproduced in pairs for the use of the stereoscope which should be used if any detail is to be obtained from the prints.

A chapter on the physiology of gastrojejunostomy has been rewritten in the light of the latest investigations. Emphasis is laid on using all the methods at hand for a diagnosis, the author advocating the generous use of the stomach-tube and the data acquired from it. The chemical diagnosis is important in conjunction with the clinical and pathological ones. The radiographic diagnostic points are also discussed and several plates are shown illustrating the same. Throughout the work the author has endeavored to give a clear-cut working plan and guide for the diagnosis and treatment of surgical conditions of the stomach.

The pre-operative care of the patient is described, and the post-operative care is given an important place and position in the management of a case. Contrary to the usual thought, the author lays a great deal of importance to the after-care and nursing in some of the conditions. Early feeding in debilitated cases, attention to physiology of the diaphragm, exercising it with deep res-

pirations, active use of the stomach-tube for vomiting, retention, and distention, all bear great weight in turning the balance in favor of the patient.

The author's views on some of the present-day mooted points are formulated with a view to the welfare of the patient rather than to merely follow out theories based on broad statements made by some writers on insufficient data. The discussion on gastrojejunostomy and on congenital pyloric obstruction bears this out.

The reviewer has read the work with a great deal of interest and benefit.

E. L. E.

THE POSTURE OF SCHOOL CHILDREN. By JESSIE H. BANCROFT, Assistant Director Physical Training, Public Schools, New York City. New York: The Macmillan Company.

THERE is a field in which it is possible to accomplish great good, and that field includes the vast majority of children from four to fifteen who are never instructed at home in the art of correct poise of the body. The writer feels that in this mission this book can prove its maximum value. If children can be taught from the time they first begin to walk until fifteen years of age how to walk, stand, and sit correctly the postural deformities of adolescence will be reduced to a minimum. This book is capable of teaching mothers of average intelligence to so train their children that when the age of puberty arrives such children will not only be saved from the debilitating results of faulty posture, but will have gained a robustness that will withstand a greater measure disease.

W. J. M.

SYNOPSIS OF SURGERY. By E. W. H. GROVES, M.S., M.D., B.Sc., F. R.C.S., Surgeon to the Bristol General Hospital; Consulting Surgeon, Cossham Hospital; Lecturer on Surgery at Bristol University. Fourth Edition. Pp. 582, with illustrations. New York: William Wood & Co., 1914.

A BOOK that has reached its fourth edition is its own recommendation, and this is no exception. The important new features of this edition are the rewritten sections on pathology and bacteriology, and the addition of the newest theories of shock, the newest means of anesthesia and nerve surgery.

The book is a synopsis; dealing with statements of facts arranged in a rational, clear, and concise manner, especially good for students and practitioners. The book is not a treatise of surgery,

it is merely a systematic grouping of all the important facts from diagnosis to treatment. Operations are not described in detail but merely the salient facts are given; in this way impressing the important features on the student's mind and not losing him in a mass of detail.

In size, binding, and contents the book is ideal for students' use. It is complete, accurate, with all useless theories eliminated and has a pleasing, forcible style. E. L. E.

INSURANCE MEDICINE. By HENRY H. SCHROEDER, M.D. Pp. 150.
New York: William Wood & Co.

THIS little volume comprises a series of articles which have appeared in the *Medical Record*. The large insurance companies work up medical statistics at the present day with care and thoroughness from an enormous mass of material in which the individuals can be traced for years, and the conclusions drawn are of interest and importance to the general medical world. Of particular interest in Dr. Schroeder's book, is a consideration of the comparative longevity of individuals showing abnormally heavy or unduly light body weight, as observed at various ages.

This book is worthy the attention of any practitioner who may be occasionally called upon to make an insurance examination, and its perusal may serve to clear up some of the misunderstandings which so frequently occur between the examiners and the medical department of an insurance company. R. G. T.

THE ELEMENTS OF BANDAGING FRACTURES AND DISLOCATIONS.
By WM. RANKIN, M.A., M.B., Ch.B., Dispensary Surgeon,
Western Infirmary, Glasgow, etc. Pp. 116; 68 illustrations.
London: Henry Frowde & Hodder & Stoughton, 1913.

THIS little book is intended solely for students and those practitioners with a very limited experience. It endeavors to give in detail those important features in the bandaging of fractures and dislocations that are not mentioned in the larger works. The work can by no means be regarded as a complete treatise on any of the subjects discussed, nor is it intended to be. Many very good minor points are depicted in the text and illustrations. In order, however, to warrant calling the work one on *Bandaging of Fractures and Dislocations*, the author should have given much more attention to bandages and their application in his text. E. L. E.

PROGRESS
OF
MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

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Studies on the Coagulation of the Blood, with Special Reference to Endemic Goitre.—J. BAUER and M. BAUER-JOKL (*Ztschr. f. klin. Med.*, 1914, lxxix, 13) have investigated the coagulability of the blood, particularly in diseases of the thyroid gland, since Kothmann and Lidsky in 1910 reported delayed coagulation in hyperthyroidism and rapid coagulation in hypothyroidism. They used the method of Fuld. Bauer and Bauer-Jokl find that there is almost always a delay in the coagulation time of patients with goitre regardless of the functional activity of the gland. The determination of the coagulation time, they find, is not of differential diagnostic value in hyper- and hypothyroidism. A prolongation of coagulation time is very common also in various other affections of the glands of internal secretion as well as in general neuropathy and in status hypoplasticus. In all these conditions the delay in coagulation is coincident, usually, with a lymphocytosis or mononucleosis or even an eosinophilia. After strumectomy and thymus resections in three cases, there was observed a marked decrease in the coagulation time. Administration of thyroid extract in moderate doses may decrease the time. In a case of hemophilia with infantilism due to thyroid disease, thyroid extract had a marked effect; before administration the blood was not completely clotted after fourteen hours, but after giving the gland, coagulation occurred in twelve minutes. The delay in coagulation in disturbances of the glands of internal secretion, and in status hypoplasticus is attributable, Bauer and Bauer-Jokl believe, to abnormality in ferments. A delayed coagulation time is also found in nephritis, in various anemias, and in diseases of the liver.

Studies on the Concentration of the Blood Serum in Anemias and Diseases of the Blood.—It has been maintained by Grawitz that the blood serum in pernicious anemia is relatively rich in protein, while in anemias of malignant or septic origin there is a marked hydremia. He has also claimed that the serum of chlorotics is comparatively rich in protein as compared to post-hemorrhagic anemias. Naegeli has apparently disproved this by studies of the viscosity of the sera. E. HEUDORFER (*Ztschr. f. klin. Med.*, 1914, lxxix, 103) has studied the question through determination of the protein content of the serum by means of the Pulfrich refractometer. His calculations have been based on the tables of Reiss. He has studied four cases of chlorosis, eight of pernicious anemia, five of secondary anemia, one of hemolytic anemia, four each of myeloid and lymphatic leukemia, four of polycythemia, four of anemia from malignant disease, and three with lymphogranulomatosis. The pathologically increased concentration of the serum was found in no instance. A decrease in concentration was not unusual. The most marked hydremia was found in chlorosis and pernicious anemia, while with malignant tumors, this was less striking. While no far-reaching conclusions can be drawn from the few observations made, still it is apparent that the protein concentration of the serum is not of differential diagnostic value in chlorosis, pernicious anemia, and anemia of malignant disease.

Determination of Blood-sugar Under Normal and Pathological Conditions.—H. G. BING and B. JAKOBSEN (*Deutsch. Arch. f. klin. Med.*, 1914, exiii, 571) have studied the blood-sugar quantitatively by Bang's method. They find that the normal percentage is between 0.06 and 0.12, the average being about 0.1. After administration of 100 gm. glucose there is generally a well-marked increase, though at times it is lacking in normal individuals. One finds a similar rise after ordinary food. Hyperglycemia is often found in patients with nephritis, not necessarily associated with hypertension. In the cases of neurasthenia, hyperthyroidism and gastric diseases studied, no hyperglycemia was found, though it was present in connection with diseases of the pancreas. In diabetes Bing and Jakobsen found hyperglycemia after meals and during fasting periods, but there was no direct relationship between the degrees of hyperglycemia and glycosuria. In some cases of glycosuria and in some cases of diabetes mellitus, the estimation of the blood-sugar was of prognostic value.

The Demonstration of the Liver and Spleen by the Röntgen Rays.—C. LÖFFLER (*Münch. med. Woch.*, 1914, lxi, 763) describes a procedure for demonstrating the liver and spleen with the röntgen rays. It is also of advantage in detecting gall-stones and alterations in the gall-bladder. The patient fasts the day before the examination is made. The large intestine is then emptied by enemata, and gas is introduced by a rectal tube. The quantity of air or gas required for a picture of the spleen is less than for the liver, for in the former case it is only necessary to distend the colon as far as the splenic flexure. In the plate the spleen appears as an equilateral triangle about the size of a boy's hand, whose base is parallel to the lateral abdominal wall, while the apex—corresponding to the hilus—points toward the median line. Both

sides of the triangle are somewhat concave. In demonstrating the liver the gas should extend to the cecum, and the stomach is distended in the usual manner. The entire organ is well shown by this procedure. Care should be exercised in cases where there is definite ulceration in the stomach or intestines.

On the Relationship of Positive Venous Pulse and Tricuspid Insufficiency.—J. NEUMANN (*Deutsch. Arch. f. klin. Med.*, 1914, cxiv, 484) notes the swing of the pendulum in the interpretation of the positive venous pulse. Up to 1906 it was looked upon as diagnostic of tricuspid insufficiency, but since 1909 its interpretation has been in more or less doubt, since it was shown that inactivity of the auricles in the absence of tricuspid insufficiency might also lead to a positive pulse in the veins. Neumann's studies led him to conclude that the positive venous pulse which accompanies perpetual arrhythmia permits one to make no definite diagnosis for or against tricuspid insufficiency in such a case. The positive venous pulse may, however, be diagnostic of a tricuspid lesion under the following conditions: (a) If the positive venous pulse is very strong or can be palpated, or if a tone can be heard over the vein, or if the liver pulsates, tricuspid insufficiency can be diagnosed. (b) If the positive venous pulse is only slightly evident, possibly not visible without retraction of the head, then a tricuspid insufficiency may be excluded. Neumann points out that the combination of a positive venous pulse with regular rhythm of the heart is with few exceptions indicative of an insufficiency of the tricuspid valves.

On the Distribution of Glucose in the Blood.—H. TACHAU (*Ztschr. f. klin. Med.*, 1914, lxxix, 421), employing his own method, has studied the distribution of sugar in the blood. Lépine and his co-workers have assumed that, in addition to free sugar, there is combined sugar in the blood which becomes free within one-quarter of an hour after the blood is drawn. Tachau has investigated this point. He found in some cases that there is a distinct rise after the blood has stood one hour, amounting to as much as 10 per cent., though in other instances this was entirely lacking. He, therefore, devised a procedure by which he could make immediate examinations. In the blood of the fasting patient, Tachau found that the plasma showed a somewhat higher concentration in glucose than the whole blood or corpuscles. At the height of alimentary hyperglycemia, the difference between plasma and whole blood was considerably greater in many instances. In other cases, however, even an hour after taking the carbohydrate there was no difference from the condition found in the fasting patient. Calculations of the sugar content of the red blood corpuscles showed that there was a marked rise in most cases during alimentary hyperglycemia. Only in a few instances did the sugar concentration in the corpuscles remain relatively low and in one instance no sugar was found in them. A certain time after the taking of carbohydrates a lower concentration was found in the plasma than in the whole blood. Tachau advises the use of whole blood in the study of alimentary hyperglycemia.

SURGERY

UNDER THE CHARGE OF

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Paravertebral Anesthesia in Gall-stone Surgery.—JURASZ (*Zentralbl. f. Chir.*, 1914, xli, 1409) ascribes the success of paravertebral anesthesia largely to the fact that large quantities of non-toxic novocain with adrenalin can be employed. The fluid is injected in the neighborhood of the spinal ganglia and the intervertebral foramina. It had been considered necessary to inject on both sides in order to obtain sufficient anesthesia for abdominal operations. The method has been employed for operations in the neck, thorax, and abdomen. Francke observed severe collapse in several cases and thought this was due to rapid and wide extension of the anesthetic fluid over the surface of the dura mater. Kappis also observed collapse, but in only mild grade in two out of 30 cases. Jurasz does not believe it is due to an epidural extension of the anesthetic fluid but to a special intolerance of some patients especially, to strongly concentrated solution of novocain. He believes that too much demand is made by some surgeons on the tolerance of the body to this substance which is a poison. He recommends its employment in gall-bladder surgery, especially for cases in which general anesthesia is contra-indicated. He employed it in two cases without further anesthesia of the skin or peritoneum and obtained complete anesthesia of the abdominal walls, the peritoneum and right-sided abdominal organs. Operative shock, also, seemed to have been excluded completely. He employed the following technique: With the patient in the left lateral position and the knees drawn up, a small quantity of a 0.5 per cent. novocain in solution is injected subcutaneously in a line about 3 cm. from the spinous processes. Then in this line at the level of the sixth spinous process, a fine long needle is introduced and made to seek the lower border of the corresponding transverse process. Close under it the needle is passed about 0.5 to 1 cm. deeper in a slightly median direction and is moved about carefully until the patient experiences a pain radiating forward. Then 5 c.c. of the solution are deposited without changing the position of the needle. The pain ceases completely in a minute. The needle is then allowed to remain in position and a second needle is employed to make a similar injection at the level of the next spinous process. After this injection the first needle is removed and with it a third spinal nerve is injected in the same way, the second needle remaining in position. In this way the necessary number of spinal

nerves are anesthetized. In the lower breast region the spinous processes do not guide the point of injection because the lower transverse processes are more at a right angle with the vertebrae. Here, the best guide is the distance between the upper punctures. Patience is necessary on the part of the surgeon and patient because it is not always easy to find the nerve and the patient must put up with considerable pain. Injection on both sides is not necessary and for that reason this method is suitable for operations on the liver and gall-bladder. The injection of 40 c.c., which Jurasz employed in both of his cases, will produce no symptoms of shock.

Permanent Drainage in Ascites.—OBERST (*Zentralbl. f. Chir.*, 1914, xli, 1465) says that the methods of permanent drainage of ascites which have won a permanent place for themselves, are the Talma operation, the modified Eck fistula between the portal vein and vena cava which can be employed only rarely, and the various methods for discharging the fluid into the subcutaneous tissue. In the latter group foreign bodies have been employed, as drainage buttons of glass, drainage tubes, silk threads, etc. Oberst proposes the use of a piece of the skin instead of a foreign body, the skin being suited to permanently conduct the ascitic fluid into the subcutaneous tissue. In an overhanging part of the abdomen, *e. g.* in the midline below the umbilicus after the removal of the ascitic fluid, a transverse flap of skin is outlined by the knife. This is about three inches from above downward and about six inches from side to side, larger on the left than the right side. The larger left half is separated from its bed, while the small right half is left attached for nourishment. The separated portion is now doubled on itself so that the skin surface presents on all sides and its edges are united by sutures. This flap is then passed through a small laparotomy opening into the abdomen and fixed in this position by a few sutures at its base. The edges of the surrounding skin wound are now undermined and brought together over the central skin flap. Because the edges of the laparotomy wound cannot unite with the sunken skin covered flap, the ascitic fluid will continuously escape into the subcutaneous tissue. Instead of doubling the flap, one may roll the detached portion into the form of a tube with the skin inside or out, and suture it in the laparotomy opening. The principle is the same to prevent the closing of the opening between the abdomen and subcutaneous tissue by interposing a skin covered flap. The operation can be done under local anesthesia. The laparotomy opening should be small to prevent the escape of intestines, a small opening being sufficient for the escape of the ascitic fluid. The first method of using the skin flap worked best.

Cleft Palate and its Treatment.—DRACHTER (*Deut. Zschr. f. Chir.*, 1914, cxxxi, 1) divides the methods of treatment in vogue into (1) those which bridge over the cleft, (2) those which fill it, and (3) those which approximate its margins. The cleft upper jaw is abnormally wide, the average increase in width between the alveolar processes being 0.8 cm. In a unilateral cleft the palatal plates are of normal width, but they are more oblique than the palatal plates of the normal

upper jaw. The individual variation in the angle of inclination of the palatal plates varies within the same limits (20 degrees) as under normal conditions. The variation in the width of the cleft is greater. The distance between the margins of the gap in the palatal plates is called the absolute width of the cleft. The distance between the mucosa covered margins of the cleft is called the "relative width of the cleft." The "absolute" cleft does not correspond to the increase in the alveolar distance. The former is much greater than the latter. As a rule the width of the cleft depends upon the abnormally oblique palatal plates. A parallel approximation of the opposite halves of the upper jaw until the cleft margins are in contact must, therefore, result in a pathological narrowing of the upper jaw, especially, when one or both sides are turned inward. The abnormal inclination of the palatal plates is not so marked that a turning down of flaps from mucous membrane and periosteum to a more horizontal position, suffices to cover the cleft. Only in certain cases with oblique palatal plates and a mild absolute cleft will it be possible to bridge the cleft in this way. The usual form of absolute cleft is that with parallel margins. When the cleft edges are approximated, the uvula will be angular and not rarely in the median line. After the edges of a hare-lip have been united, very regularly, the margins of the cleft uvula tend to turn toward each other and the complete cleft can be changed into an incomplete one, the cleft in the hard palate becoming narrowed. Also in a double complete cleft after uniting the margins of the hare-lip, the alveolar portion of the cleft can close spontaneously after a time. It is of importance to study the form of the absolute cleft before the hare-lip operation, immediately after it, and some years afterward. The cleft afterward changes in size, becoming smaller for a time and advantage should be taken of this fact. The modern methods of operation for approximating the alveolar processes (Brophy, Shoemaker) should not be recommended. They are dangerous and often fail. Forcing the two sides together until the margins of the cleft are approximated, will make the upper jaw abnormally narrow and will cause a faulty position of the intermaxillary bone. Nor are the non-operative methods of approximating the halves of the upper jaw to be recommended because they bend the alveolar processes inward making the obliquity of the palatal plates greater and increasing the deformity. By both methods the development of the teeth is very much interfered with or prevented by the wire necessary for the approximation and the cleft is not completely closed. The Langenbeck operation will still be necessary for this purpose. Drachter recommends that incomplete clefts be closed by the Langenbeck operation. Unilateral complete clefts should be allowed to change after the performance of the hare-lip operation, in which case the intermaxillary bone will take its normal position. Bilateral complete clefts should also be aided by the effects of the hare-lip operation. In those cases with a projecting intermaxillary bone the latter should be displaced backward by the Bardeleben operation, before the hare-lip operation is performed. The cleft in the hard and soft palate should be closed at about the end of the first year or beginning of the second, when the best effects of the preceding hare-lip operation will have been obtained. At this period, after the Langenbeck operation, a combination of the approximation of the cleft margins and a bridging of the cleft, should be provided.

THERAPEUTICS

UNDER THE CHARGE OF

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The Influence of Intravenous Injections of Hypertonic Salt Solution in Pulmonary Hemorrhage.—MOCZULSKI (*Wien. klin. Woch.*, 1914, xxvii, 613) says that intravenous injections of 10 c.c. of a 10 per cent. salt solution had striking results in nine cases of pulmonary hemorrhage. The effect is not immediate and such injections do not prevent a recurrence of the hemoptysis. In purpura and similar hemorrhagic affections, the author observed no favorable influences from these injections.

Mixed Starch Diet in Diabetes Mellitus.—FALTA (*Münch. med. Woch.*, 1914, lxi, 1218) advocates a diet of mixed starches to combat acidosis in diabetes mellitus, instead of confining the carbohydrate to a single form of starch as is the case with the use of oatmeal as advocated by von Noorden, or the "potato cure." The principle of his method is that carbohydrates are given liberally in the form of different starches only. Falta makes use of gruels or soups of rice, corn, barley, tapioca, potato, spaghetti, noodles, or various starches made into crackers or bread. The practical importance of such a diet is that it is not so monotonous as the oatmeal diet and can be given over longer periods of time. The author emphasizes the importance of excluding from the diet all forms of animal albumen such as meat, eggs, cheese, milk, etc. "Vegetable days" or "fasting days" are interposed between periods of liberal feeding and are most important in order to secure the best results. Falta says that, theoretically, the presence of animal albumen in the diet diminishes the formation of glycogen in the liver and consequently more sugar passes through the liver into the blood. In severe diabetes, the organism is unable to use this sugar on account of pancreatic insufficiency. Falta has obtained striking results in the treatment of severe diabetes by a diet on these principles. The diet must be persisted in for often the results at first are not marked, but careful and persistent dieting leads to permanent improvement.

The Treatment of Scarlet Fever with Salvarsan.—LEUZMANN (*Therapie d. Gegenwart*, 1914, iv, 243) reports excellent results with the use of neosalvarsan for the treatment of scarlet fever. He makes use of a solution of 0.15 gm. of neosalvarsan in 5 c.c. of a sterile 0.4 per cent. salt solution, using correspondingly larger amounts of the salt solution for larger doses of salvarsan. This solution is injected by preference intravenously, although in very young children, where intravenous injections are difficult, it can be given intramuscularly. Leuzmann advises small initial doses; beginning with 0.15 gm. and

this dose should only be increased when there are no untoward by-effects and when no marked rise of temperature follows the injection. He says that severe types of the disease should be treated with especial caution with regard to the dosage. The maximum single dose for children from three to eight years of age should be 0.15 gm.; for children from eight to fifteen years, 0.3 gm., and for adults, 0.45 gm. However, these higher doses should not be given as the initial dose, and lately the author has been in the practice of giving even to adults a dose of 0.15 gm. at the beginning of treatment, and if this dose is well borne it is gradually increased to the maximum. Leuzmann has treated 47 cases of scarlet fever by this plan and he is convinced of the therapeutic value of the treatment. He gives temperature charts and details of four of these cases in his article.

The Intraspinal Use of Salvarsanized Serum.—McCLURE (*Boston Med. and Surg. Jour.*, 1914, clxxi, 520) reports the results in 9 cases of syphilis of the central nervous system in which the salvarsanized serum was employed according to the technique of Swift and Ellis. Improvement in the subjective and objective symptoms was obtained in 4 cases of cerebrospinal syphilis under treatment with intravenous injections of salvarsan, mercurial inunction, and the intraspinal use of salvarsanized serum. With this improvement there was a diminution in the cell count, the protein content, and the strength of the Wassermann reaction in the spinal fluid. The Wassermann reaction in the blood remained unaffected up to the time of leaving the hospital. Two cases of tabes were relieved of subjective symptoms and the number of cells in the cerebrospinal fluid reduced. A case of tabeto-paresis showed no change in the laboratory findings and only slight improvement symptomatically. One case of paresis showed marked improvement in the symptoms and in the laboratory findings. The Wassermann reaction became negative in the spinal fluid. One case of paresis showed no improvement in either the symptoms or the laboratory findings, but progressively grew worse. McClure says that the results in cerebrospinal lues and tabes of this method of treatment in his series and those collected from the literature are encouraging not only as regards cessation of symptoms but also in the laboratory findings in the cerebrospinal fluid. The results in paresis are either discouraging or problematical. The most marked improvement has occurred in the laboratory findings and in these there has been a relapse in those cases followed for several months. The improvement in mentality so far recorded may be but the result of remissions to which the disease is prone, even in the absence of treatment. However, the fact that improvement may occur even if only apparent, warrants the use of the intraspinal treatment in a disease otherwise hopeless.

Treatment of Tetanus with Subcutaneous Injections of Magnesium Sulphate.—FALK (*Deutsch. med. Woch.*, 1914, xl, 1689) says that the subcutaneous injection of magnesium sulphate for the treatment of tetanus is especially adopted for use in field hospitals and so may have a wide application in the present war. The subcutaneous use of magnesium has been very limited in Germany. Stadler reported 4 cases

treated by this method, 3 of these being tetanus neonatorum, all of which ended in recovery. The intraspinal method has been more widely applied in Germany. This treatment, according to Stadler, was successful in two-thirds of the cases treated. Of five especially severe cases treated in the Turco-Bulgarian war two recovered. Falk says that the subcutaneous injection of magnesium seems to be especially successful in tetanus neonatorum. This treatment limits the convulsions so that feeding is possible and pain is relieved and in consequence the patients sleep. The danger of the use of magnesium is its depressing effect on respirations and, in 2 cases this effect was so pronounced as to threaten life. The fatal result in these 2 cases seemed to be averted by the intramuscular injections of calcium chlorate as advised by Meltzer. In the third case the magnesium treatment was confined with chloral hydrate administered by rectum and recovery was uneventful. When magnesium is given subcutaneously severe depression of respiration is uncommon according to the reported cases. Magnesium sulphate should never be given intravenously as even small doses may prove fatal. Falk says that in America the adult dosage is from 8 to 20 grains daily, the number of injections being three a day. Solutions of magnesium sulphate in concentrations of from 10 to 40 per cent. have been used. Stadler believes that the injection of solutions of from 30 to 40 per cent. strength is far less painful than the weaker solutions. The solutions are easily made and can be readily sterilized; the same is true of solutions of calcium chlorate.

Clinical and Experimental Observations on the Action of Salvarsan on Syphilis of the Fetus by Treatment of the Mother.—MEYER (*Münch. med. Woch.*, 1914, lxi, 1801) has treated a number of syphilitic pregnant women with salvarsan and gives his findings from both a clinical and chemical standpoint especially as regards the action of the drug on the placenta and fetus. He found that the arsenic content of the placenta corresponded with that of the maternal blood circulating in it. An intact placenta is not permeable to arsenic. A syphilitic placenta may be traversed by arsenic but the frequency with which this occurs is unknown. Success in the treatment of a syphilitic fetus with salvarsan depends upon successful treatment of the maternal syphilis and is probably prophylactic rather than remedial. The drug is well tolerated by pregnant women. Intravenous injection does not produce abortion or hemorrhage. Death of the fetus after intravenous injection of salvarsan has never been observed by Meyers. In a series of 37 syphilitic pregnant women treated energetically with salvarsan combined with mercury, living children were born in 97.4 per cent. In a series of 43 women so treated, 86 per cent. of children were alive on the tenth day and 15.8 per cent. of children gave a positive Wassermann reaction at birth. However, the number of children with a positive Wassermann reaction does not comprise the total number of cases of congenital syphilis and he believes that all children of a syphilitic mother should be treated with antilactic treatment even if there are no chemical or serological evidences of syphilis.

PEDIATRICS

UNDER THE CHARGE OF

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Impaired Resonance at the Apices in Children.—FR. MIELKE (*Berlin klin. Woch.*, 1914, li, 1218) contributes interesting investigations bearing on the diagnosis of impaired apical resonance in children, and offers 18 cases to illustrate his points. In many poorly developed children with pallor and loss of appetite, an impairment at one apex would generally indicate apical tuberculosis. If, besides this, there is a poor family history, a positive Von Pirquet or possibly elevated temperature, the diagnosis would seem to be confirmed. On closer study these children are found to exemplify a type characterized by muscular weakness and poor development of the spine and back. In standing they exhibit a marked lordosis with often a slight kyphosis of the lumbar vertebra. The conformity of the vertebra is still infantile and in this position a slight scoliosis exists. Asked to stand erect the child leans back still farther, increasing the scoliosis. Even a small bending of the vertebral column in a small, elongated thorax will cause a shortening of the percussion note at the apex. If the child's position be corrected by having him lean forward slightly, the arms hanging loosely downward and the abdomen drawn in, the muscles of the thorax will be relaxed, the spine straightened, and on percussion of the apex the impairment present in the erect position will have disappeared. This would indicate that an impairment is only significant when it persists in the corrected posture. Roentgen-ray plates of these cases show the first three ribs lying closer together than normal and the first rib sunk inward, thus narrowing the upper thorax aperture. This fact, coupled with the crooked posture due to muscular weakness, explains the production of the pseudo impairment. The 18 cases cited clearly demonstrate Mielke's contention as most of them seem tuberculous from their general symptoms and the impairment present in the uncorrected posture, but in all of them the impairment disappeared in the correct posture, and roentgen-ray examination showed no pathological change in the lungs, even in cases showing a positive von Pirquet, an elevated temperature, or a tuberculous family history. Mielke suggests that this method applied to apparently tuberculous children might lower the statistical incidence of tuberculosis in childhood.

Three Cases of Acute Lymphatic Leukemia in Children.—MARSH (*Liverpool Medico-Chirurg. Jour.*, 1914, xxxiv, 324) reports 3 cases of acute lymphatic leukemia in children of eleven, four and three years, respectively. Many cases escape recognition because, without a hematologic examination it is almost impossible to differentiate this condition from hemorrhagic purpura, scorbutus, and hemorrhagic septicopyemic conditions. The onset is usually sudden, but may be insidious with weakness, fever, lassitude, and dyspnea. The most striking

manifestation is the hemorrhagic diathesis causing hemorrhages into the subcutaneous tissues and bleeding from the mucous membrane of the mouth, the nose, and the urogenital and gastro-intestinal canals. The characteristic feature in the blood is the great increase in the lymphocytes with a preponderance of the large variety. The percentage of lymphocytes in the cases recorded by Marsh is 93 per cent. and 94 per cent. Petechiae occurred in all the cases, but the spleen was not enlarged. The enlargement of the lymph nodes is never as marked as in the chronic form of leukemia. Other clinical features of the disease are lymphoid infiltration of the liver with consequent enlargement, progressive emaciation and cachexia, increased secretion of uric acid and in most cases moderate fever, often typhoid or septic in type. The reported cases all died within two or three weeks of the onset of the acute symptoms. Two cases followed the extraction of a tooth which seemed the start of the bleeding from the mouth. Horse serum, arsenic and rest had no effect on the course of the disease. Röntgen-ray therapy in a few cases has caused a reduction in the lymphocytes to normal or below, and diminished the size of the lymph nodes and liver temporarily, but this was always followed by a very rapid return of all these conditions followed by death in all the cases. The generally accepted view of the etiology of the disease, is that it is caused by some toxins manufactured within the body.

The Incidence of Pulmonary Tuberculosis in Children.—McLELLAN (*Liverpool Medico-Chirurg. Jour.*, 1914, xxiv, 333) makes deductions on the incidence of pulmonary tuberculosis in children from the recent investigations in this field. It is fairly generally accepted that the vast majority of children under the age of twelve years have been subjected to the attack of the tubercle bacillus. In regard to the von Pirquet test McLellan states the belief that as proof of active tuberculosis after the age of three years the test is unreliable. Also that the younger the child the greater the reliance that may be put on the results and that in most cases the only deduction that may be drawn from a positive result is that the patient at sometime or other has been subjected to the attack of the tubercle bacillus. While Moreland's modification of the von Pirquet is most hopeful, no specific method has been devised by which to definitely decide whether the disease is in an active or passive condition. The opinion held by McLellan that glandular infection is a common occurrence and pulmonary tuberculosis is rare, he admits is not shared by the majority of practitioners. Large numbers of children are admitted to hospital with the diagnosis of phthisis, who have slight catarrhal symptoms or glandular involvement and who respond rapidly to ordinary hygienic and medicinal treatment and show no evidence of the disease clinically. McLellan's experience leads him to believe that as far as the lungs are concerned, practically all children suffering from tuberculosis die sooner or later from that disease. The first check on the diagnosis is the discovery of the bacillus in the sputum. The second check is the progress of the disease. While the very frequent cases of fibroid and bronchiectatic affections show the so-called classical signs of tuberculosis, they show the following essential differences from phthisis: No tubercle bacilli are ever found in the sputum.

The process is essentially a chronic one, the cases going on three or more years with only slight alteration in the physical signs. Lastly, the child looks healthy, its cheeks are red, its appetite good, and it puts on weight. These conditions are much more common in children than is supposed and are frequently mistaken for phthisis. Tuberculous disease of the lungs is usually secondary to diseased thoracic glands and is comparatively infrequent, but very fatal.

Psychotherapy in Childhood.—F. HAMBURGER (*Wien. med. Woch.*, 1914, lxiv, 1314) gives an excellent analysis of the treatment of psychical abnormalities in childhood. Based on the fact that these conditions depend in their development on the disposition of the child, in the sensitiveness of its nervous system and the activity of its imagination, and on an irritating cause or psychical trauma, the treatment divides itself into etiologic, prophylactic, and symptomatic therapy. The etiologic treatment depends on finding out by careful anamnesis what the psychical trauma was or is, and then try to eliminate it. The vaso-neurotic type is especially amenable to this treatment and liable to psychical trauma. In this type of child, if no murmurs are heard over the heart area, the vasomotor symptoms are usually due to a psychical cause. The severe attitude or discipline of a tactless school teacher or apparent, or real neglect or unjust severity on the part of a parent are examples of psychic trauma in such cases. The prophylactic treatment aims to change the disposition, making the child less sensitive and more self-reliant. In this respect the child is "hardened;" attempt is made to undeceive his illusions, to accustom him to disappointments, and through a firm but loving training accustom him to meet difficulties and rebuffs. The symptomatic treatment is based on the fact that the psychical trauma acts like a foreign body, the voluntary or involuntary remembrance of which is continually calling forth the symptoms of the condition. This is best relieved by diverting the mind to other things. The best method is the so-called "awake" or "alert" suggestion, by constantly holding up before the patient the ultimate, complete cure of his ailment. This is embodied in various medicaments, believed by the child and the mother to have curative properties. In addition a change in environment will aid diversion and reiteration of the statement of ultimate recovery and gaining the child's confidence by tactful kindness, with a free discussion of his condition and an answering of all questions asked will have a beneficial effect on his symptoms.

The House-fly and Diarrheal Disease Among Children.—ARMSTRONG (*Jour. Amer. Med. Assoc.*, 1914, lxii, 200) in describing an interesting experiment on the relation of summer diarrhea especially in infants, and the disease carrying properties of the house-fly, states that so far scientific field studies of this problem have been made only in the southern states. Two areas in New York City were selected. These areas were inhabited entirely by Italians, contained the same number of families under identical conditions of poor sanitation and environment. One area was left undisturbed by sanitary innovations, except that of investigating the cases of illness, their type, etc. In the other area every effort was made to eliminate the house-fly and break the

contact made between filth and food by this medium. Careful records of all the facts of morbidity and mortality in the two areas were made weekly for a period of eight weeks. In comparing these records, it is seen that the greatest emphasis must be placed on those dealing with diarrheal diseases of infants. Severe diarrheal disturbances in the protected area, in children under five years, totalled 20 cases, in the unprotected area 57 similar cases. The average case duration in the one area was 13.75 days, in the other 16.33 days. In the protected area 110 cases of sickness were recorded, in the unprotected area 165 cases. Of the infants in the protected area 88 were breast-fed and 14 bottle-fed, in the unprotected area 85 were breast-fed and 15 bottle-fed showing that this factor was practically identical. While it is believed that the elimination of flies had a great deal to do with the reduction of diarrheal diseases in children, there is no doubt that the sanitary improvement had a beneficial effect on the general physical welfare in the area. The results show that greater emphasis should be laid on the housefly in relation to diseases of children in the education of mothers, and that this should become a more important factor in infant welfare work.

OBSTETRICS

UNDER THE CHARGE OF

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The Shape of the Fetal Skull in Cases of Contracted Maternal Pelvis.—WALCHER (*Zentralbl. f. Gyn.*, 1914, No. 22) calls attention to the familiar fact that in primipara, having contracted pelvis, where the pelvis has sufficient capacity to permit the child's head to enter, that the head is usually deep in the pelvis at the end of pregnancy. This often develops as early as six weeks before the beginning of labor. In these cases the actual expulsion of the child is frequently rapid. The cranial bones are pressed under each other less than in some other cases, and the configuration of the fetal skull at birth is a close reproduction of the shape of the pelvic cavity. An exact mold of the fetal head soon after birth gives an accurate reproduction of the pelvic shape.

Cesarean Section and the Wertheim Operation, For Pregnancy with Carcinoma.—BERECZ (*Zentralbl. f. Gyn.*, 1914, No. 22) describes the case of a patient, aged thirty-seven years, multipara, with carcinoma of the cervix. The child was extracted by abdominal section, followed immediately by the Wertheim operation. A drain of iodoform gauze was placed in the pelvis, and the peritoneum closed above it. The mother made a good recovery, and six weeks after operation was given treatment by radium to prevent a recurrence. Sarwey, in Veit's *Gynecology*, has collected twenty-nine cases of carcinoma complicating pregnancy, treated by the Wertheim operation with good results. In discussion, Tauffer and others reported good results by this method of operation.

Rupture of the Uterus Treated by Operation.—AVARFFY (*Zentralbl. f. Gyn.*, 1914, No. 22) reports two cases of spontaneous rupture of the uterus treated by supravaginal amputation with vaginal drainage. In discussion others reported similar cases, in some of which drainage for supravaginal amputation was carried out through the cervix. Three of such cases resulted favorably. It was found that the indiscriminate giving of pituitrin was resulting in spontaneous rupture of the uterus, and this practice was distinctly condemned. Scipiades had treated 9 cases of uterine rupture during the last four years, 5 of which were operated upon, 56 per cent. Of the remaining 4 one was moribund when seen, one had already become infected through foul amniotic liquid, and was treated by drainage through the tampon with recovery. Of the 5 cases operated upon 2 died, having had complete rupture of the uterus before admission, and brought to hospital in a dying state. Of the 3 which recovered 2 had complete rupture and 1 incomplete. When a comparison is made between the results obtained by drainage with the tampon and operation it is observed that where drainage is possible it gives as good results as operation, and that many cases cannot be treated by operation, where a small percentage can be saved by the use of the tampon. Tauffer had obtained good results by drainage with the tampon, and had reduced in his clinic the percentage of operations by this method.

Eye Lesions Produced by Pregnancy and Labor.—ADAM (*Monatsschrift f. Geb. u. Gyn.*, Band 39, Heft 6, 1914) observes that albuminuric retinitis is a frequent complication of nephritis. In 935 pregnant women suffering from kidney lesions there were 209 cases of retinitis, 22.4 per cent. Those patients having chronic interstitial nephritis have these lesions most often. Less frequently it occurs in acute nephritis, and is also seen in the anemic form of so-called kidney of pregnancy. The general clinical picture is such that a diagnosis can usually be made without the use of the ophthalmoscope. When examination is made the lesion is usually found in the region of the macula, and may be difficult to detect because the pupils are strongly contracted. In these cases the pupils are best dilated by two drops of a 1 per cent. homatropin solution, or two drops of 5 per cent. cocain. Atropin should not be employed, because it disturbs the muscles for some time afterward. The first symptom usually described by the patient is that of a dark speck before the eye. The patient can move about a room, but finds difficulty in reading and writing. In rare cases complete blindness may develop. Where this is one-sided it indicates plugging of the central artery of the retina on that side. Where it is bilateral it indicates uremia. Where a portion of the field of vision is greatly distorted, separation of a portion of the retina or plugging of the central vein has occurred. These patients also see specks and distorted beams of light before the eyes. When the eyes are examined lesions are found as well in the optic nerve, as in the retina. The head of the optic nerve is much reddened and swollen, but not to that extent seen in acute syphilis. The papilla is usually surrounded by a clear space, which extends into the retina. The central vessels show alterations in caliber, the arteries being contracted, the veins dilated. This is the result of inflammation in the nerve which compresses the

arteries, and also prevents a discharge of blood through the veins. The lesions in the retina, especially found in the macula, are small white areas connected with greater or smaller hemorrhages. The figure of a star, often described as seen in these cases, is not common. In albuminuric retinitis there are no pigment changes, and this constitutes a point of differentiation in diagnosis between syphilitic lesions of the retina, where changes in the pigment are pronounced. As a complication, separation of the retina is often observed. This is detected through the grayish color of the retinal tissues with the dilatation and dark appearance of the vessels. Occasionally the central artery or vein is plugged. Where the artery is occluded the posterior portion of the eye is gray in color and in the region of the macula shows cherry-red blotches; while in cases where the veins are plugged, there are areas of extravasated blood. After the disease has reached its acute point the extravasated blood is in large part absorbed, but the whitish areas remain, a portion of them permanently. The swelling of the nerve subsides and is followed by atrophy. As in all inflammation, the connective tissue disappears to some extent, and there is also atrophy of the nerve fibers, with increase in connective tissue between the nerve bundles. The borders of the papilla become ill-defined through the overgrowth of surrounding tissue. Permanent lesions of the vessels are not infrequent. Examination of the whitish bodies show fatty degeneration, and osmic acid shows the formation of fatty tissue in the inner layers of the retina. This attacks the vessels most in the form of endarteritis. The prognosis of albuminuric retinitis complicating pregnancy is always doubtful as regards the preservation of normal vision. It is exceptional for the eyes in such a case to completely recover. Where the retina separates in pregnant patients, the prognosis is much better than in the non-pregnant, for it often adheres again. So far as the prognosis for life is concerned, this complication is not especially threatening, it does not indicate so grave a condition in the kidneys as when it develops in the non-pregnant. Where a patient has had nephritis before pregnancy the prognosis is less favorable. As regards treatment, the majority believe that albuminuric retinitis complicating pregnancy indicates the interruption of pregnancy. This advice is most valuable when pregnancy is interrupted immediately after the beginning of the first eye lesions. Where retinitis has gone on for some time the interruption will not have much influence for good. It is of the utmost importance that patients be guarded from retinitis and that severe nephritis be treated promptly by the interruption of gestation. When the mother declines to abandon pregnancy and accepts the risk of impaired sight, an absolutely hopeless prognosis must not be given. Patients must be warned against repeated pregnancy, as repeated retinitis is especially dangerous to vision. In some uremias sudden blindness develops. Here one finds in the posterior portion of the eye no distinct lesion, in spite of the blindness the pupil reacts and the lesion must be considered cerebral. When the uremia is improved by treatment the vision usually returns to normal. In eclampsia one observes sudden blindness developing, as in uremia. Most of these patients are so mentally disturbed that they have no sensation of vision, where they are conscious they assert that after a brief period of impaired vision they have seen alterations

in color, followed by sudden blindness. With the ophthalmoscope nothing is often found in the eye to account for this condition. The writer has examined in the University Frauenclinic of Berlin, 92 cases of eclampsia. In 44 there was disturbance of vision, in 4 retinitis or neuroretinitis. In these cases albumin did not disappear from the urine after confinement, while in the other cases it entirely ceased to be present as soon as the uterus was emptied. The 4 cases may be classed as nephritic, the remaining 88 as typical eclamptics, of whom 40 had disturbance of vision. In most of these cases there was complete amurosis in a smaller proportion pronounced amblyopia. In these cases the amurosis had previously existed and had grown somewhat better at the time of examination. In all these cases the pupil reacted promptly, showing the lesion to be cerebral. In the majority of patients blindness and unconsciousness persisted together for hours and sometimes for days, but normal vision returned in those who recovered. In 36 cases examined by the ophthalmoscope, the findings were normal, and in 4 cases there were lesions not previously described. In some portions of the periphery the fundus was dark, and in these portions the vessels stood out more prominently. Unless the eye was examined carefully these lesions might not have been noticed. In other portions it was possible to make out sclerotic vessels resembling those seen in syphilis and arteriosclerosis. An opportunity occurred to examine one of these eyes postmortem, and lesions were found in the iris and in the vessels of the iris. Where these lesions in the iris were observed, the prognosis was worse than where they were absorbed, as in the 4 cases two terminated fatally, indicating the severity of the toxemia. In general it may be said that the more sudden and intense the disturbance of vision in eclamptic patients the more favorable is the prognosis for subsequent normal sight.

GYNECOLOGY

UNDER THE CHARGE OF

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"Koagulen" as a Hemostatic in Gynecology.—ALBRECHT (*Zent. f. Gyn.*, 1914, xxxviii, 1185) has tried the substance prepared by Fonio under the name of "Koagulen" in the treatment of various forms of hemorrhage that are of interest to the gynecologist. This material is a powder, the result of fractional centrifugation of animal blood, and is supposed to contain in concentrated form the coagulation-stimulating properties of the blood-platelets. The powder is dissolved in normal salt solution just before using, so as to make a 10 per cent. solution. The cloudy fluid thus resulting is boiled for two to three minutes, and is then ready for use. It may either be applied to the bleeding area by means of a syringe or by soaking sponges in it, and then pressing them firmly for a few moments to the site of hemorrhage. Albrecht has found it of great value in controlling the often very troublesome oozing occurring from raw surfaces after breaking up intestinal and adnexal adhesions in inflammatory cases. Such hemorrhages are, as every

surgeon knows, at times exceedingly difficult to control, often requiring more time and labor than all the rest of the operation; it is just these cases that Albrecht has found "Koagulen" most useful, as it in all instances caused rapid and permanent cessation of bleeding of this character. On hemorrhage from actual arteries or veins of any size, however, on atonic uterine hemorrhage, or in fact metrorrhagia of any type, it apparently had little or no effect, and he saw no value from its use in plastic work, nor in any vaginal operations.

Formalin in the Treatment of Uterine Hemorrhage.—GERSTENBERG (*Zent. f. Gyn.*, 1914, xxxviii, 1201) is a strong advocate of the use of pure formalin in the treatment of excessive uterine hemorrhage, of the "idiopathic" type, claiming that it is simpler, cheaper, and just as efficient as the röntgen ray, and far safer than zinc chloride, atmokausis, and other methods of violent cauterization that have been suggested. He says that he has been using formalin for this purpose since 1900, and has had only two failures, in one of which there was an endometrial polyp, and in the other small myomata. His technique is to wrap a very small bit of cotton about a fine Playfair sound, soak this in full strength formalin solution (40 per cent. formaldehyde gas), and then gently pass it through the internal os, bringing it in contact with as much of the endometrial surface as possible, but removing it before any contraction takes place in the cervix. After about five minutes any such slight cramp that may occur will have passed off, and a second sound is passed in the same manner, care being taken to protect the vaginal walls by means of cotton from coming in contact with the solution. A tampon is placed against the cervix for twelve hours, to absorb any fluid that may come from the uterus, and the patient is advised to remain in bed as much as possible for the first two days, during which time no douches of any sort should be taken. Gerstenberg says he has found this treatment so effective that if two applications do not rapidly cause cessation of hemorrhage, he takes it as a pretty good indication that there is some more definite cause for the bleeding than was at first evident, such as myoma, carcinoma, etc., requiring further investigation. He has never seen any bad results follow, such as abdominal cramps, syncope, infection, stenosis, etc., the only theoretical danger being that of losing the pledget of cotton in the uterus. This has never happened to him, but did to one of his friends; after twenty-four hours it was spontaneously expelled without harm.

"Chronic Metritis."—An attempt to bring some order into our conception of this very loosely applied, and often misapplied term, has been made by SHAW (*Jour. Obst., and Gyn. British Empire*, 1914, xxvi, 74), who has made careful histological studies of a number of uteri removed under this clinical diagnosis. He believes that there are at least two, if not more, totally distinct classes of cases, so far as their etiology is concerned, that nevertheless produce a similar symptom-complex, and are therefore commonly grouped under the general designation of "chronic metritis." The attributes possessed in common by these classes are that the uterus is regularly enlarged, thick-walled, and firm, producing excessive hemorrhage, leucorrhœa, and dragging pain. The two groups that he has been able to differentiate

are: (1) the result of subinvolution of a parous uterus, and (2) due to hypertrophy of a non-parous uterus. In his study Shaw has examined 25 cases of the former and 4 of the latter condition. He has found in in each group the uterine wall grossly thickened, this thickening being due in neither case, however, to any relative increase in the fibrous tissue, as is commonly supposed, but simply to a quantitative increase in both the muscular and fibrous elements, these maintaining about their normal relative proportions. He therefore considers the term "fibrosis uteri," which some authors would apply to this condition, distinctly bad. The most marked difference between the two groups is in the elastic tissue, in the hypertrophic group this maintaining the arrangement characteristic for normal, nulliparous uteri, *i. e.*, it is confined almost exclusively to the internal elastic lamina of the blood-vessels, with only very delicate fibrils in the media and adventitia, and running out between the muscle fasciculi of the mesometrium, whereas in the subinvolution group thick strands of elastic tissue can always be found surrounding the outside of the bloodvessels and extending out through the uterine musculature. In regard to the etiology, Shaw thinks the thickening of the uterine walls is the result in the subinvolution cases of a failure of the parous uterus to return to its normal condition because of advanced age of the patient, sepsis, general ill health, etc. To account for the hypertrophic group, he advances the theory that the endometrium is the prime factor in causing the uterine enlargement. In all the cases examined the endometrium was markedly thickened; the cause of this, Shaw was not able to determine, but he believes that once this has taken place, the thickened endometrium acts practically as a foreign body in the uterus, and gives rise to excessive contractions, especially at the menstrual periods, resulting in a "work-hypertrophy" of the entire musculature. He believes that the hemorrhage in the subinvolution group is due to the excessive amount of elastic tissue present, this not having the same contractile power upon the bloodvessels as muscle, whereas in the hypertrophic group it comes chiefly from the thickened endometrium, as is evidenced by the fact that many of these cases are greatly benefited by curettage, which is practically without result in cases of the subinvolution type.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Pulmonary Anthracosis a Community Disease.—We are commonly led to believe that anthracosis, save that observed in coal-miners, is a harmless process to which all city dwellers are exposed. Such a statement, however, without qualification, is erroneous, particularly because

the character and extent of industrial development in different cities has greatly altered the quality of the air we breathe. KLOTZ (*Amer. Jour Public Health*, 1914, iv, 887) has taken advantage of the conditions of the Pittsburgh atmosphere, and in association with other studies upon the smoke problem, has made observations upon the accumulation of carbon in the tissues of the lung. By his observations no support is given to intestinal absorption of carbon as an important factor in pulmonary anthracosis. Furthermore, the presence of carbon or soot in the mouth does not lead to its deposit in the tonsils or absorption by the associated lymphatic system. Similarly the trachea and bronchi do not appear to have the power of disposing of the pigment other than incorporating it in a mucous secretion, which subsequently reaches the mouth. Owing to the system of angular and moist channels of the upper respiratory passages the greater amount of carbon is caught before reaching the lung. That which reaches the air-sacs is picked up by living phagocytes and carried into the lymphatic channels of the lobules. The larger channels in the periphery of the lobules soon show the presence of the pigment by the sharp black lines, which may be observed on the lung surface of young children. Some of the phagocytic cells carry their pigment burden to the lymph glands at the hilus, others plug the channels or lead to nodular accumulations in the ampullary portions of junction points. Obviously the amount of pigment in any lung is dependent upon the quantity inhaled, or better upon the quantity of carbon in the atmosphere of one's daily life. With the larger quantities of pigment scattered through the lung substance there is a distinct loss of elasticity of the tissue. This physical change is associated with a structural alteration, in which the most marked condition is the fibrosis about the anthracotic deposit. These fibroses are, at times, nodular or again diffuse. The air spaces are encroached upon, with the result that the less involved areas respond in compensatory emphysema. The more marked anthracotic deposit seriously impairs the function of the lung. Pleural adhesions are not developed as a result of the deposit. An interesting point was observed that the cells active in the phagocytosis of the carbon migrated to areas of chronic inflammation, particularly tuberculosis, and formed a pigmented wall about such areas. The fibrosis which accompanied these carbon deposits tended further to encapsulate the tuberculous foci. Acute inflammation (pneumonia) was not assisted in this manner, but was rather impeded in its favorable outcome during the stage of resolution. Estimates of the total carbon content of the lung were made in which quantities varying from 1.2 to 5.3 grams were obtained in individual lungs of Pittsburgh inhabitants while 0.14 and 0.4 grams were obtained in two lungs from residents in Ann Arbor, Michigan. The fact appears to be clearly borne home to us that a variable anthracosis and its sequelae affects city dwellers according to the amount of smoke pollution in their respective communities.

Rabies. JAMES J. CUMMING (*Journal of Infectious Diseases*, January, 1914, xiv, No. 1, p. 33) presents the results of his studies on fixed virus with special reference to the action of disinfectants, the effect of heat, passage through Berkefeld filters, infectivity; also the effect of dialysis and exposure of the virus to peritoneal fluid *in vivo*. Cumming furthermore determined the minimum lethal dose of the virus and gives the

results of immunity tests on sets of animals which had been vaccinated by various methods of antirabic treatment, and finally reports the results of a new method which he designates that of dialysis.

The experiments show that a 1 per cent. solution of phenol does not destroy the virus by an exposure of six hours, whereas a 2 per cent. solution kills it in less than twenty-four hours. These experiments were made by exposing the virus to the disinfectant in a test-tube, and should, therefore, not be translated to the treatment of the wound in the animal. The specific disinfecting action of formaldehyde is shown by the fact that the virulence of the virus (again *in vitro*) is lost when exposed for two hours to an 0.08 per cent. solution. As a result of this finding Cumming advises the use of formalin upon all wounds made by animals suspected of being rabid. The actual effect of formalin upon such wounds in animals was, however, not tested.

The virus is readily destroyed by heat—in twenty minutes at an exposure of 47°C ., and in less than two minutes at 100°C . In thick homogeneous suspensions the virus may be made to pass through a Berkefeld filter.

By the intracranial method of injecting the virus the mortality is 100 per cent. Next in order as to mortality is the intramuscular route—50 per cent. Intraperitoneal injections give a death rate of 15 per cent., while by the intravenous method the animal rarely dies. It was found that when the virus in collodion sacs was exposed to the peritoneal fluid its virulence was lost in from three to six hours. An interesting series of experiments was conducted to show the effect of dialyzing a fresh standard suspension against running distilled water. Under these circumstances the virus loses its virulence and it was found that the important factors in effecting the destruction of the virus were the thickness of the collodion sac, the percentage of rabid brain in suspension, and the rate of flow of the distilled water.

The minimum lethal dose of the fixed virus by the intracranial method of injection was found to be 0.5 c.c. of a 1 to 25,000 suspension in physiological salt solution. In the tabulations given it is noted that by the Högyes method of treatment the immunity conferred will protect against about 1.5 minimum lethal doses. The Pasteur treatment protects against about 2 minimum lethal doses of the fixed virus, while the vaccine prepared by the dialyzed method will protect against as much as 8 minimum lethal doses. Furthermore, the vaccine prepared by the dialyzed method will not produce the disease when injected intracranially. Cumming, therefore, claims that the subcutaneous injections of the dialyzed vaccine are entirely safe as a prophylactic measure and they confer a high degree of immunity. Over 800 persons bitten by animals suspected of having rabies have been treated by this new method at the Pasteur Institute at Ann Arbor, Michigan. In this series no cases of rabies developed.

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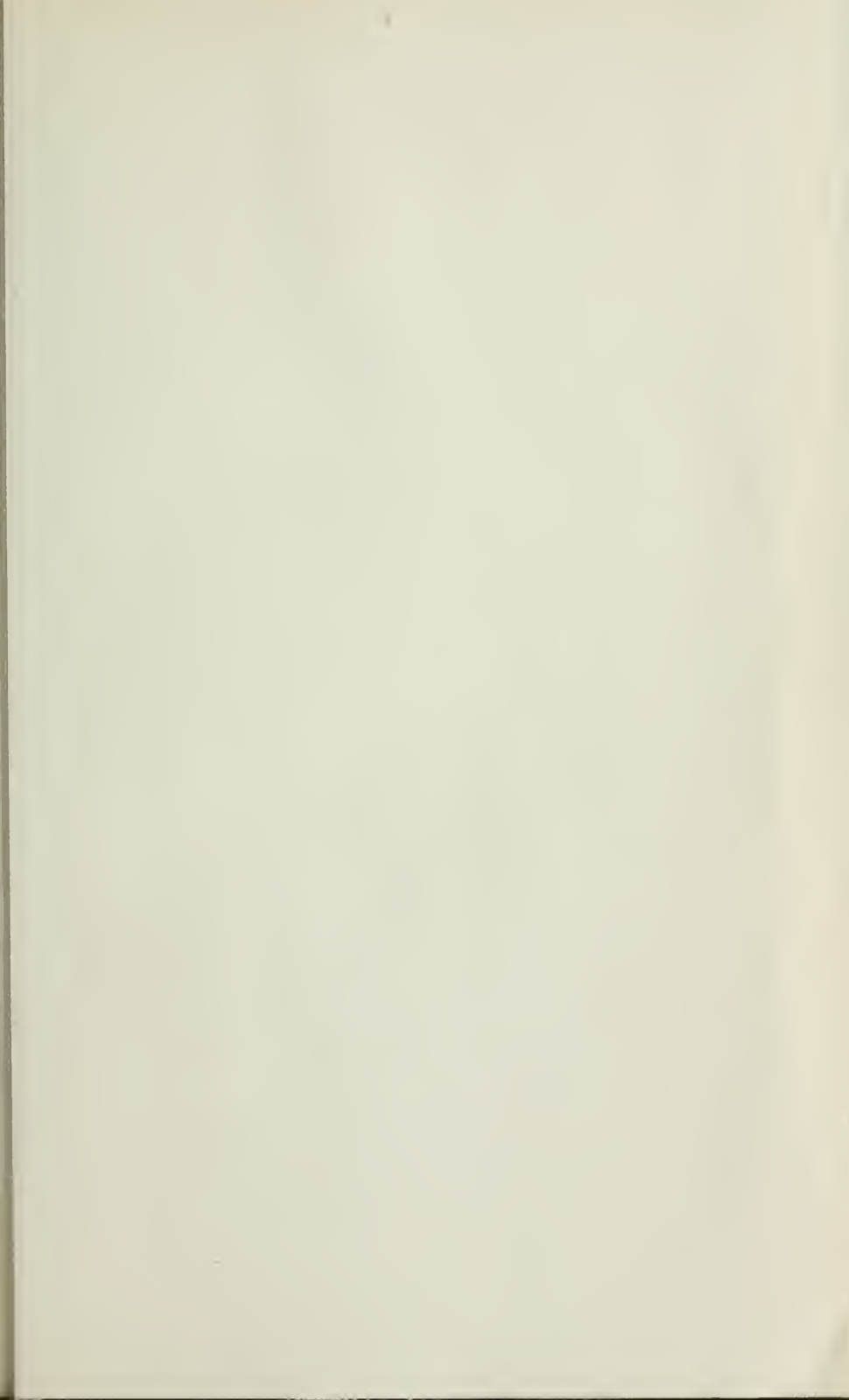
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